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**THE FRANK E. BUNTS INSTITUTE**

announces

**A Course In**

**General Diagnosis and Treatment**

on

**MONDAY, TUESDAY, and WEDNESDAY  
NOVEMBER 7, 8, and 9, 1938**

---

**A Course In**

**Diseases of the Eye**

**Will Be Given in Conjunction with the  
Cleveland Ophthalmological Society**

on

**MONDAY, TUESDAY, and WEDNESDAY  
DECEMBER 5, 6, and 7, 1938**

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**On**

**WEDNESDAY, THURSDAY, and FRIDAY  
DECEMBER 7, 8, and 9, 1938**

**The Frank E. Bunts Institute**

**Will Present a Course In**

**Diseases of the Ear, Nose, and Throat**

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**Descriptions of these courses, outlines of the subjects, and  
application blanks will be found on pages 303-308.**

## LOW BACK PAIN AND SCIATICA DUE TO PROTRUSION OF INTERVERTEBRAL DISCS

### *Report of Four Cases*

J. I. KENDRICK, M.D. AND A. T. BUNTS, M.D.

Of the several possible causes of low back pain with radiation along the course of the sciatic nerve, protrusion of a lumbar intervertebral disc is one of the most definite pathological conditions which may explain such pain. Although only a small percentage of cases of low back pain and sciatica probably can be explained on this basis, it is of great importance to bear in mind the possibility of such a condition. Within the past four years an increasing number of these cases has been reported in the literature and it would seem that the condition is of fairly frequent occurrence. The recognition of the clinical picture associated with protrusion of a lumbar intervertebral disc and the development of measures for investigating the condition have made it possible to arrive at a definite diagnosis.

The outstanding symptom is pain. This pain is severe in character and frequently is referred to the lateral aspect of the leg. On examination of the patient the following signs are significant: a decrease in lumbar lordosis, limitation of motion in flexion of the lumbar spine, and diminution or absence of an Achilles reflex. Lumbar puncture is an important procedure in diagnosis. In approximately 80 per cent of cases, the total protein content of the cerebrospinal fluid is elevated above the normal limit of 40 mg. per 100 cc. The injection of a contrast medium, such as lipiodol, into the lumbar subarachnoid space followed by roentgen examination demonstrates the protruded disc and completes the diagnosis.

Surgical removal of the protruded portion of the disc, thus freeing the involved nerve from pressure, is followed by prompt relief of pain.

The following cases present the important clinical features and roentgen findings of a protruded lumbar intervertebral disc.

### REPORT OF CASES

*Case 1:* The patient, a man 57 years of age, came to the Clinic complaining of severe pain in the right hip. This pain radiated into the entire right leg and there was severe radiation into the posterior aspect of the thigh and the lateral aspect of the leg just above the lateral malleolus. The condition began eight months previously when the patient felt something snap in his back after the extraordinary exertion of a heavy lift. The difficulty immediately following the injury consisted of stiffness and aching but there was no severe pain. Treatment had com-



### PROTRUSION OF INTERVERTEBRAL DISCS

prised a period of rest in Florida which resulted in some improvement due to the change in climate and the limited activity. Six months after the injury and two months before examination at the Clinic, the pain began to radiate into the right leg and to become very severe. The patient stated that he felt the pain must be due to a pinched nerve because it was so intense. The pain was described as burning, aching, cramping, and at times lancinating in character.

Examination revealed a well developed and nourished man whose lumbar spine was definitely flattened. There was restriction of motion in the lumbar spine in flexion and lateral bending to the right. These movements aggravated the pain. By deep palpation, tender areas were noted to the right of the fourth and fifth lumbar spinous processes. The neurological examination revealed definite hyperesthesia over the lateral aspect of the right calf and diminution in the right Achilles reflex.

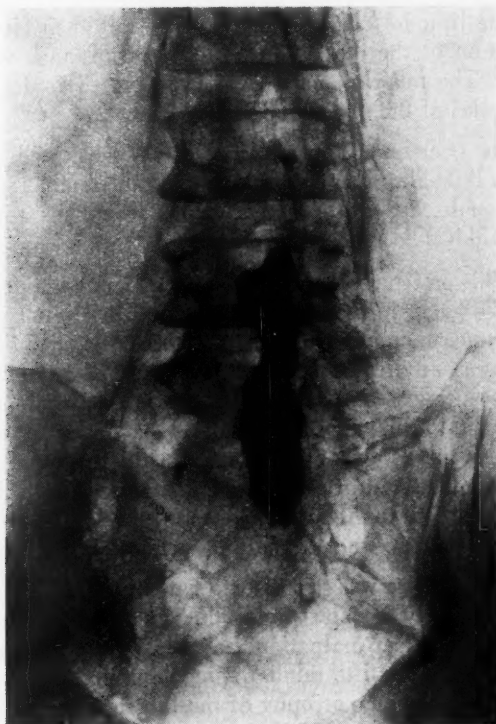


FIGURE 1: Roentgenogram showing deformity in column of lipiodol characteristic of protruded intervertebral disc between the fourth and fifth lumbar vertebrae.

A clinical diagnosis of protrusion of a lumbar intervertebral disc was made.

The patient was admitted to the hospital for further investigation. A lumbar puncture was done between the fourth and fifth vertebrae and the first 5 cc. of fluid withdrawn were sent to the laboratory for examination. The total protein content was reported as 45 mg. per 100 cc. In view of the clinical picture and the elevated protein content, the next step in the diagnosis was the injection of lipiodol into the lumbar subarachnoid space. The roentgenogram (Fig. 1) showed a deformity in the lipiodol column on the right side, adjacent to the intervertebral disc between the fourth and fifth lumbar vertebrae. This completed the diagnosis.

A laminectomy was performed with removal of the laminae of the fourth and fifth lumbar vertebrae. After removal of the laminae, a greatly thickened ligamentum flavum was noted overlying the dura. When this thickened ligament was removed, the fourth lumbar nerve was seen to be pushed backward by the protruding intervertebral disc. The dura was opened and the lipiodol removed. The dura was then closed and the herniated portion of the disc and the nuclear substance was removed extradurally. The muscles and fascia were closed in layers. There was prompt relief of the severe pain.

Three weeks after operation the patient was permitted to be out of bed. He wore a light aluminum brace to support the lumbar spine for four months and then discarded it. The patient has been back at his work for four months and has been perfectly well.

*Case 2:* This patient, a man 41 years of age, complained of pain in the small of the back, in the left hip, and down the left leg. The onset dated back sixteen months at which time stiffness and dull aching developed following any exertion. With the onset of warm weather, the patient had a remission of symptoms and not until five months previous to examination and following the lifting of some heavy kegs and tubs of ashes did the soreness in the back recur. At this time the radiation of the pain began. The pain was severe and radiated down the posterior aspect of the left thigh to the lateral aspect of the leg. The leg was described as feeling numb and the pain as aching and cramping.

On examination there was noted some flattening of the lumbar spine. Flexion movements of the spine were limited and these movements aggravated the pain. By deep palpation, an area of tenderness was made out just to the left of the fifth lumbar spinous process. The neurological examination revealed some atrophy of the left thigh and calf, hyperesthesia over the lateral aspect of the leg, and diminution of the left Achilles reflex.

### PROTRUSION OF INTERVERTEBRAL DISCS

A clinical diagnosis of protrusion of a lumbar intervertebral disc was made.

The patient was admitted to the hospital and a spinal puncture was done between the fourth and fifth lumbar vertebrae. Examination of the first 5 cc. of fluid withdrawn showed the total protein content to be 45 mg. per 100 cc. Following the injection of lipiodol into the lumbar

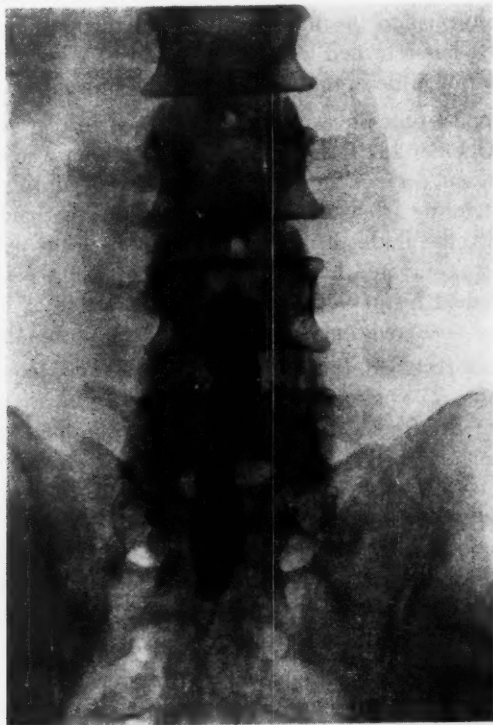


FIGURE 2: Roentgenogram showing deformity in column of lipiodol characteristic of protruded intervertebral disc between the fifth lumbar vertebra and the sacrum.

subarachnoid space, roentgenograms (Fig. 2) revealed a deformity in the lipiodol column on the left side adjacent to the intervertebral disc at the lumbosacral junction. This completed the diagnosis.

A laminectomy was performed, removing the lamina of the fifth lumbar vertebra and a portion of the sacrum. The ligamentum flavum was considerably thickened. The dura was exposed and opened and the lipiodol removed. The fifth nerve was retracted to the right and the disc protrusion was removed. The sheath of the nerve was thickened from the

pressure of the thickened ligament and protruding disc. The dura was closed and the muscles and fascia closed in layers. There was prompt relief of the severe pain.

Three weeks after operation, the patient was out of bed wearing a light aluminum brace to support the lumbar spine. The brace was worn for four months and then discarded. He has continued to have some numbness in the left leg but none of the severe pain. A complete range of motion has returned to the lumbar spine and no pain followed these movements. He has returned to light work and is anxious to resume his former occupation which requires considerable physical exertion.

*Case 3:* A 38 year old white man was seen in the Orthopedic Department on October 11, 1937. His chief complaint was of pain which had been present for six months. The pain was dull and steady in character, extending from the right buttock down the back of the right thigh and leg to the ankle; it was most noticeable in the popliteal space. The pain was aggravated by arising from the sitting position. There was no antecedent history of trauma. No disorders of micturition or defecation had occurred and he had experienced no numbness.

Examination revealed limitation of forward and lateral flexion of the lumbar spine. The patient had a tendency to stand with a slightly backward curve of the lumbar spine. Roentgen examination of the lumbosacral region and of the sacro-iliac joints revealed no abnormality. At that time the condition was considered to be a mechanical strain of the back for which a Williams brace, baking, and massage were prescribed. After three months, the pain continued to be just as severe as formerly and a sacro-iliac belt was then applied but this failed to give relief even after four months. In the meantime the patient had resorted to various osteopathic and short-wave treatments without relief.

On May 9, 1938, the patient was re-examined. The forward and backward movements of the lumbar spine were still definitely restricted and the lumbar lordosis was absent as before. The patellar and Achilles reflexes were equal and active. There was less than one-half inch of atrophy of the right thigh, but the right calf showed one inch of atrophy. Investigations for a protruded lumbar intervertebral disc were then carried out. Lumbar puncture between the third and fourth lumbar vertebrae and examination of the cerebrospinal fluid showed a total protein content of 50 mg. per 100 cc. which was definitely above the normal limit. Through a spinal puncture needle, 5 cc. of heavy lipiodol were then injected into the spinal subarachnoid space between the first and second lumbar vertebrae. Fluoroscopy and roentgenograms revealed a definite deformity in the right side of the column of opaque

### PROTRUSION OF INTERVERTEBRAL DISCS

material at the level of the interspace between the fourth and fifth lumbar vertebrae, representing a protrusion of the intervertebral disc (Fig. 3).

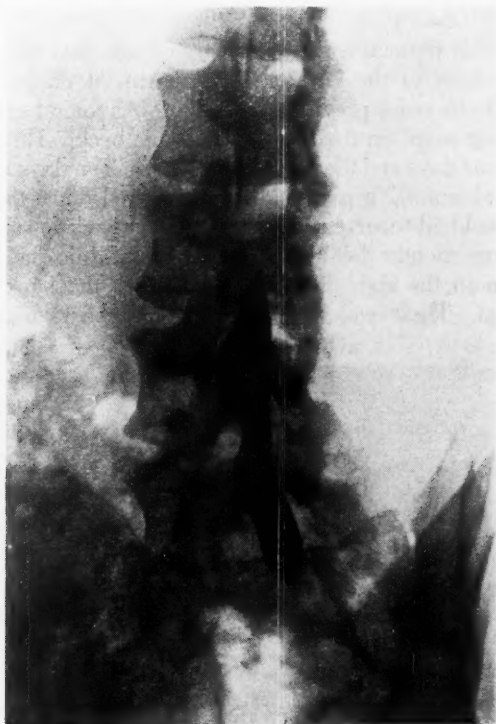


FIGURE 3: Roentgenogram showing deformity in column of lipiodol characteristic of protruded intervertebral disc between the fourth and fifth lumbar vertebrae.

Laminectomy of the fourth and fifth lumbar vertebrae was performed on May 11, 1938. A markedly thickened ligamentum flavum was found to be compressing the dural sac and there was a protrusion of the intervertebral disc between the fourth and fifth lumbar vertebrae, causing compression of the fourth lumbar nerve root on the right side. The hypertrophied ligamentum flavum and the protruded portion of the intervertebral disc were removed, and the nerve root was thus released from pressure. Through a small opening in the dura the lipiodol was removed by irrigation and aspiration.

The postoperative course was uneventful, the wound healed well, and the patient was discharged from the hospital on the twenty-first

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postoperative day. He has remained entirely free from his former pain ever since the operation. He wore a light brace for four months and then discarded it. When he was last seen on September 8, 1938, four months after operation, he was in good health and free from pain. There was a good range of motion of the spine in all directions.

*Case 4:* This patient, a man 39 years of age, was first seen by Dr. James A. Dickson of the Orthopedic Department on June 28, 1938. He stated that ten years previously, while doing some heavy lifting, he "felt something snap" in the lower part of his back. He rested in bed for three or four days and then returned to work. Ten days later, the pain was entirely absent. No pain had been referred down the leg. Since that time he had had recurrent pain in the lower back for several days at a time. Three months before coming to the Clinic, he began to experience pain in the right hip, radiating down the back of the right thigh and leg. There was a sensation of numbness over the lateral

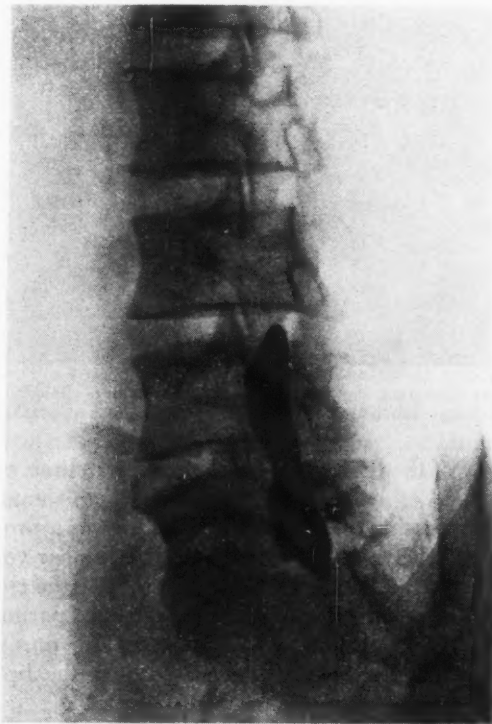


FIGURE 4: Roentgenogram showing deformity in column of lipiodol characteristic of protruded intervertebral disc between the fourth and fifth lumbar vertebrae.



### PROTRUSION OF INTERVERTEBRAL DISCS

aspect of the right lower leg. The patient had been obliged to spend most of his time in bed during the two weeks before he came to the Clinic.

Examination showed marked restriction of all movements of the lumbar spine, especially of flexion. There was three-fourths of an inch of atrophy of the right thigh and calf. Flexion of the right hip with the right leg extended was impossible because of pain. The patellar and Achilles reflexes were equal and active.

Roentgenograms of the lumbosacral region revealed nothing of pathological significance.

Spinal puncture between the third and fourth lumbar vertebrae and examination of the cerebrospinal fluid showed a total protein content of 55 mg. per 100 cc., which is definitely above the normal limit. An injection of 5 cc. of heavy lipiodol into the spinal subarachnoid space was then made between the first and second lumbar vertebrae. Roentgen examination showed a deformity in the right side of the column of opaque material at the level of the interspace between the fourth and fifth lumbar vertebrae, characteristic of a protruded intervertebral disc (Fig. 4).

Laminectomy of the fourth and fifth lumbar vertebrae was performed on July 11, 1938. A thickened ligamentum flavum was removed from its position overlying the dura. Extradural exposure of the right fourth lumbar nerve showed that the nerve was compressed between the thickened ligamentum flavum and a protruded intervertebral disc. After the ligamentum flavum had been removed, the protruded portion of the intervertebral disc was entirely removed and the fourth lumbar nerve was thus freed from compression. The lipiodol was removed by irrigation and aspiration through a small opening in the dura. Following operation, the patient made a satisfactory convalescence and he has remained entirely free from his former pain.

The patient will continue to wear a light brace for three or four months after operation and will then discard it.



## MESENTERIC VENOUS THROMBOSIS WITH OPERATION AND CURE

### *Report of a Case*

WILLIAM E. LOWER, M.D. and McCLEERY GLAZIER, M.D.

Mesenteric vascular occlusion is considered by most authorities to be a relatively rare disease. This condition was first described by Triedman in 1843 and Virchow described its pathology in 1847 but not until 1895 when Elliott reported his case was operation first carried out successfully. Since 1895 there have accumulated numerous case reports, classifications, and theories regarding its etiology, frequency, and symptomatology. The purpose of this paper, however, is not to review the literature but to report a case which presented an interesting problem in diagnosis and treatment.

### REPORT OF CASE

The patient was a white, married man, 39 years of age, whose occupation was inspector of golf clubs. He entered the Clinic on Dr. William J. Engel's service complaining chiefly that rather severe, constant pain in the epigastrium had been present for 20 hours.

*Present Illness:* About 20 hours previously, while working, this patient had a sudden attack of acute pain in the upper part of the abdomen; the pain did not radiate but remained localized. It was not colicky in nature and within a few minutes subsided to a dull ache. Since the onset, he had experienced acute exacerbations which necessitated morphine for its relief. There was no immediate associated nausea or vomiting but a few hours after the onset the patient stated that a small amount of the contents of the stomach had been vomited. There was no hematemesis. There was no previous history of stomach trouble or disease of the gallbladder. He had never been jaundiced and there had never been acholic stools. He gave no history of attacks of appendicitis previously and this pain was not associated with diarrhea, constipation, or blood in the stools. The bowels had moved the afternoon of the day of onset but had not moved the day of entrance to the Clinic.

*Past History:* The past history and history by systems revealed no significant findings. As stated previously, the patient denied having had disease of the stomach or gallbladder, and there was no history of cardiac pathology or blood dyscrasia. He absolutely denied previous illness in any form.

*Physical Examination:* The patient was a well developed, fairly well nourished, white man, of about the stated age, who appeared to be

## MESENTERIC VENOUS THROMBOSIS

experiencing quite severe abdominal pain. The skin was somewhat cold and clammy, the temperature was 98.4° F., the pulse rate 72, respirations 20, and blood pressure 145 systolic, 100 diastolic. The pupils were pinpointed and did not react to either light or accommodation. The patient had received one-fourth grain of morphine about one hour before entering the Clinic. Otherwise the eyes were entirely normal. The findings of the remainder of the examination of the head and neck were entirely within normal limits.

The chest was symmetrical and expansion was equal; the lungs were clear to auscultation and percussion; there was no dullness or tubular breathing; the mediastinum was negative. The heart was not enlarged and there were no murmurs; the sounds were of good quality, the rate was 72, and the rhythm was normal. The peripheral vessels were apparently normal.

The abdomen was moderately distended throughout and mildly spastic above the umbilicus. There was no rigidity and no definite point of maximum tenderness to palpation, but the patient complained of generalized soreness while being examined. No scars and no masses were present. The liver edge could not be felt; the gallbladder and spleen were not palpated.

Rectal examination gave entirely normal findings; the prostate was normal in size, shape, and consistency. Neurological findings were all within normal limits; no pathological reflexes could be elicited.

The clinical impression of the examiner was: (1) subacute perforated peptic ulcer; (2) subacute pancreatitis; (3) volvulus; and (4) Meckel's diverticulum.

*Laboratory Studies:* Examination of the urine showed the reaction to be 5.5; there was four plus albumin with numerous hyaline and granular casts, 10 to 12 red blood cells, and 3 to 5 white blood cells per high power field. Examination of the blood showed 5,700,000 red cells, 23,150 white cells, 100 per cent hemoglobin, 85 per cent neutrophils, 13 per cent lymphocytes, and 2 per cent monocytes. The level of the blood sugar was 152 mg. and of the blood urea 54 mg. per 100 cc. two and one-half hours postprandial. The Wassermann and Kahn tests gave negative reactions.

It was the impression of the referring physician, Dr. N. Kiefer, Geneva, Ohio, that this was possibly an atypical attack of renal colic and he requested complete urological examination which was carried out immediately by Dr. Engel. A routine plain film of the kidneys, ureters, and bladder was entirely normal except that the roentgenologist stated that there was considerable gas in the upper portion of the intestines. Cystoscopic examination gave entirely normal findings.

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Catheters were passed to both kidney pelves and a bilateral pyelogram showed both pelves to be normal.

About four o'clock in the afternoon the patient was admitted to the hospital for observation. He was made comfortable with hot stupes to the abdomen and a rectal tube to relieve the distention. No morphine was given at this time. About three hours after admission, the temperature rose to  $101.4^{\circ}$  F., the pulse rate was 128, and respirations 24. At this time, the patient was in quite severe pain, the pain being confined particularly to the upper part of the abdomen and epigastrium. As before, the pain did not radiate but remained localized and was not associated with nausea, vomiting, or diarrhea. The abdomen was definitely spastic in its upper half but quite soft and distended in the lower half. Percussion revealed free fluid in the right flank. No board-like rigidity was present and no masses were palpable. It was our impression that, although the findings were certainly not typical of a perforated viscus, this was the most probable intra-abdominal pathology.

At 8:30 in the evening, about four and one-half hours after admission, Dr. William E. Lower performed an exploratory laparotomy, using a right paramedian incision. Upon opening the peritoneum, there was a gush of approximately 2000 cc. of blood-stained abdominal fluid which had the consistency of a transudate. Upon removal of this fluid, the presenting loop of bowel was seen to be definitely injected and distended, but no evidence of an exudative peritonitis could be seen. The mesentery of this loop was found to be apparently normal. This loop of bowel was examined proximally where it was found to be entirely normal. The stomach, gallbladder, and duodenum were likewise normal. The liver was palpated and was found to be normal. The presenting loop of bowel was then examined distally where, about midway in the ileum, it was found to merge with a loop of bowel approximately 18 inches long which was reddish-purple in color with petechial hemorrhages over the serosa of the bowel. It was moderately distended and the mesentery of this segment was of a purplish-blue color with dilated veins; the mesentery was definitely thickened and edematous. No arterial pulsations were palpated and although the veins were dilated they were not indurated. There was no evidence of torsion of this involved segment of gut. Distal to this involved segment the small intestine again became apparently normal with the exception of moderate injection of the serosa; the bowel was collapsed and the mesentery apparently was normal. The large bowel was entirely normal and collapsed.

It was the impression of the surgeon that this lesion was one of beginning intestinal gangrene due to vascular occlusion; however, it was impossible to state whether the occlusion was arterial or venous in

## MESENTERIC VENOUS THROMBOSIS

origin. The operation consisted of resection of the involved segment of bowel, care being taken to remove all the involved mesentery and bowel. The resection was carried out into normal tissue. The mesentery was then approximated by means of continuous chromic catgut sutures and an end-to-end anastomosis of the cut ends of the bowel was performed by the closed method. About eight inches above the anastomosis an ileostomy was performed for the purpose of decompressing the bowel and to relieve tension on the suture lines. The abdomen was closed without drains.

The patient was placed immediately upon a strict Alonzo Clark routine with continuous stomach suction. Adequate fluids were given parenterally. The following morning his condition appeared to be fair, his temperature was 101° F., pulse rate 140, and respirations 28. The abdomen was flat and the Wangensteen was functioning properly as was the ileostomy. During the course of the day he remained in fairly good condition but that afternoon his temperature rose to 104° F., pulse rate to 160, and the respirations were 32. Examination of the abdomen at this time revealed mild distention but no rigidity. It was felt that this reaction was probably due to a beginning peritonitis so the parenteral administration of sulfanilamide with equal amounts of sodium bicarbonate intravenously was prescribed. The initial dose was 90 grains daily for the first 48 hours which was followed by 60 grains every 24 hours thereafter for the following three days and then it was discontinued. Mild acidosis developed and this condition was combatted by means of the intravenous administration of sodium bicarbonate. The number of white blood cells dropped to 9000 with 85 per cent neutrophils and remained at about this level for the following five days.

During the first three postoperative days, the evening temperature rose to about 104°F. with tachycardia in proportion to this elevation; however, the temperature began to approximate normal thereafter and on the fifteenth postoperative day the highest elevation was 99.5° F. and on the nineteenth postoperative day it became normal and has remained so.

On the fourteenth postoperative day, because of the immense loss of fluid through the ileostomy, it was closed by means of four interrupted chromic catgut sutures.

The patient was discharged from the hospital on the thirty-first postoperative day. The pulse, temperature, and respirations were normal, his abdomen was flat, and he was gaining in weight and strength. The bowels moved daily, aided occasionally by small enemas. He showed a mild secondary type of anemia and this was being corrected by

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means of ferrous sulphate given orally and Parke-Davis A-B-D capsules. Chemical study of the blood gave entirely normal findings.

In conclusion, we believe that this case is one of early mesenteric venous thrombosis because:

1. Microscopic sections through the involved bowel and mesentery showed extensive edema, extravasation of blood in the tissues, and venous engorgement. There was no evidence of ulceration of the mucous membrane of the bowel, a condition which is manifested relatively early in arterial occlusion.

2. The presence of 2000 cc. of blood-tinged abdominal fluid.

3. The realization that wet gangrene occurs with arterial occlusion but always following a primary ischemic gangrene and that, if this condition existed in this case, we should expect to find ulcerative lesions in the mucosa of the bowel.

## THE TREATMENT OF UNDULANT FEVER WITH SULFANILAMIDE

### *Report of a Case*

RUSSELL L. HADEN, M.D.

Undulant fever is a serious disease of great clinical importance. It is probable that acute cases occur much more often than is recognized. Chronic undulant fever is a frequent cause of an unexplained elevation of temperature.

The symptomatology of the acute and chronic types is not characteristic. In acute cases the disease may be suspected from the unexplained fever, the sweating, joint pain, and negative physical examination. The causative organism is difficult to grow in blood cultures. The agglutination test is usually positive and often to a high dilution. In chronic undulant fever the organism is also difficult to isolate and agglutination tests are often negative. Here, intradermal tests and the determination of the degree of phagocytosis of the organisms by the patient's leukocytes help greatly in making the diagnosis.

Even if the disease is suspected and the diagnosis is correctly made, the treatment has been very unsatisfactory. A specific vaccine may help in the acute form and specific and nonspecific vaccines, and induced hyperpyrexia seem of value in the treatment of some cases of the chronic type. Recently, sulfanilamide has been used in the treatment of acute undulant fever with very promising results. Stein and Blake<sup>1</sup> have reported three cases so treated with prompt clinical cure. Blumgart<sup>2</sup> has added another case successfully treated and has collected 13 cases treated by nine authors in Europe with apparent cure.

We have recently used sulfanilamide in the treatment of a patient suffering from acute undulant fever and rapid recovery has resulted.

### REPORT OF CASE

A laborer was admitted to the Cleveland Clinic complaining of cough and pain in the chest. He stated that he had had a nonproductive cough for five weeks and that coughing produced a substernal pain. He had lost 23 pounds in weight and had become increasingly weak. He had had frequent chills followed by severe sweating since the onset of his illness. He had never been ill before.

On examination his temperature was 100° F. and the pulse rate 104. The lungs were clear on examination and the heart was negative. There were no significant findings otherwise. A special examination of the nose and throat revealed nothing of significance. The urine showed a heavy trace of albumin but no casts, pus cells, or red cells. The blood



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count showed 4,280,000 red cells, 83 per cent hemoglobin, and 5,200 white cells with the following differential count: neutrophils, 62 per cent; lymphocytes, 37 per cent, and monocytes, 1 per cent. The blood urea was 30 mg., and the blood sugar 98 mg. per 100 cc. The blood Wassermann and Kahn tests gave negative reactions. The blood serum agglutinated *Brucella abortus* in a dilution of 1:2560. The blood culture was negative. A roentgenogram of the chest revealed no abnormalities.

The day following admission to the hospital, the temperature was as high as 102.2° F. Treatment with sulfanilamide was begun at once, 20 gr. being given with an equal amount of sodium bicarbonate every four hours day and night. The following day the sulfanilamide level in the blood was 19.5 mg. per 100 cc. The dose of the drug was decreased to maintain the concentration at 7 to 8 mg. The temperature returned to normal in one week and has remained so for three months. The agglutination was still positive in 1:640 dilution three months after admission. All the polymorphonuclear cells showed marked phagocytosis of *Brucella abortus* in a test of the opsonophagic power of the blood.

*Comment:* This patient lived in a country village and drank unpasteurized milk. There was no other apparent source of infection. It is possible that the cure of this patient was spontaneous but this is very unlikely. There is every probability that the cure was due to the sulfanilamide.

In giving sulfanilamide, it is most important to administer enough to keep the level of the blood constantly at the optimum level. The drug is excreted rapidly so should be given at least every four hours. We have found that 15 to 20 grains need be given at intervals of every four hours during the active stage of the infection. It seems evident that sulfanilamide is the treatment of choice in acute undulant fever.

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## SUDDEN VASCULAR OBSTRUCTION OF THE CENTRAL VESSELS OF THE EYE

### *Report of 2 Cases*

A. D. RUEDEMANN, M. D. AND R. J. KENNEDY, M. D.

When the eye is involved in a vascular accident, the treatment and prognosis always constitute a serious problem. After even small hemorrhages the eye rarely returns to normal and with a massive hemorrhage, a large percentage of the vision may be lost. Sudden loss of vision is usually due to thrombosis of the central vein or embolus of the central artery. The diagnosis is easily made by ophthalmoscopic examination as is illustrated by the following two cases.

### REPORT OF CASES

*Case 1:* The patient was a white man, 50 years of age, who was first seen on August 22, 1938. Ten days before examination, he first noticed dimness of vision in the right eye. This condition became much more severe the following day, and he consulted his oculist whose examination revealed the vision in the right eye to be 6/60, in the left eye 6/12, and corrected vision, right eye 6/30, left eye 6/6. The examination of the right eye had shown it to be essentially normal except for the disc which was swollen and the margin was indistinct; the blood vessels were thrombosed; there were numerous hemorrhages and a few white exudative spots. The blood pressure at that time was 130 systolic, 80 diastolic. The previous medical history was irrelevant except for a high blood pressure in 1934.

*Examination:* When the patient was seen at the Clinic on August 22, vision in the right eye was 4/60 and in the left eye 6/60 plus 1. The lids, iris, conjunctiva, and cornea were normal. The pupil of the right eye, which was round and reacted to light, measured 4 mm.; the pupil of the left eye measured 3 mm., was round and reacted to direct and consensual light stimulation. The finger tension was normal in both eyes and the muscle excursions were full. After dilatation with homatropine, examination of the fundus of the right eye showed many large and fine vitreous opacities; the disc was edematous and the veins engorged; the fundus was splashed with many hemorrhages of various sizes and shapes; the arteries were constricted and showed increased light reflex; the veins were dilated and showed an increased tortuosity. In the left eye, there were a few fine vitreous opacities; the disc was round, well defined, and of good color; the vessels were 3 to 4 with a slight increase in the light reflex; the macula was normal; no hemorrhages or exudates were seen. The visual field studies showed a

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large, relative, central scotoma of the right eye and some concentric contraction for form; the visual field studies of the left eye gave essentially normal findings.

*Diagnosis:* Thrombosis of the central vein of the right eye.

*Laboratory Findings:* Examination of the blood showed 5,350,000 red cells, 7,900 white cells, hemoglobin 91 per cent with differential count of: neutrophils 59 per cent, lymphocytes 36 per cent, monocytes 4 per cent, eosinophils 1 per cent. The level of the blood sugar three hours postprandial was 88 mg. per 100 cc. Sedimentation rate was 0.1 mm. per minute. The Wassermann and Kahn tests gave negative reactions. Urinalysis showed: pH 6.9, specific gravity 1.017, albumin negative, sugar negative. The glucose tolerance test gave findings within the limits of normal.

*Consultations:* This patient was referred to Dr. A. Carlton Ernstene of the Medical Department, and a diagnosis of early generalized arteriosclerosis was made. The blood pressure at this time was 128 systolic, 86 diastolic. Roentgen examination of the chest was essentially negative. The examination of the ear, nose and throat by Dr. Paul Moore showed some chemical irritation of the throat with the tonsils as a possible focus of infection.

*Treatment:* The treatment advised was deep heat to the orbit in the form of diathermy.

*Prognosis:* Poor for the right eye.

*Case 2:* This patient was a white man, 24 years of age, who was first seen on August 26, 1938. He complained that loss of vision had been present for three weeks. On August 5, while driving his car, he first noticed cloudy vision in the left eye, and two days later there was almost total loss of vision in this eye.

*Examination* revealed the vision to be 6/6 in the right eye and limited to hand movements in the left eye. Finger tension was normal in both eyes. The pupils were round and equal and reacted to light and accommodation. After dilatation with homatropine, examination of the fundus of the right eye revealed the media to be clear, the disc round, well defined, and of good color, and the lamina cribrosa visible. There were no lesions of the macula or periphery. In the left eye, there were many large vitreous opacities and the detail of the fundus was somewhat difficult to make out due to intense vitreous haze. The disc could not be outlined but was of a rosy color; no cherry-red spot could be seen in the macula although there appeared to be an area of exudate. The entire retina was ischemic. The arteries were quite small; the veins were normal in size.

## SUDDEN VASCULAR OBSTRUCTION OF CENTRAL VESSELS OF EYE

*Diagnosis:* Embolism of the central artery of the left eye.

*Laboratory Examinations:* Examination of the blood showed 5,650,000 red cells, 7,250 white cells, 95 per cent hemoglobin with the following differential count: neutrophils 57 per cent, lymphocytes 42 per cent, eosinophils 1 per cent. The level of the blood sugar 5 hours postprandial was 140 mg. per 100 cc.

*Consultations:* Examination in the nose and throat department, by Dr. Paul Moore, revealed chronic tonsillitis and a deviated nasal septum. It was felt that the tonsils might be a possible focus of infection. Examination in the genito-urinary department revealed a normal prostate.

*Treatment:* The patient was advised to have all foci of infection removed and to have deep diathermy to the orbit.

*Prognosis:* Poor. After 24 hours of anemia, the retinal tissue rarely recovers.

### COMMENT

Retinal viability is very low as is all cerebral tissue. Therefore, total anemia of the retinae for even a very short period of time is sufficient to cause its death. In Case 1 some blood still reaches the retinal tissue and if it is possible by the use of diathermy, vasodilators, sweats, etc., to open the venous outflow, some restoration of vision is possible. Usually, this does not take place and blindness ensues. The further complication is secondary glaucoma for which enucleation is advised, other measures being of almost no value. This complication occurs in 25 per cent of cases. Undoubtedly, the end result in central venous thrombosis is dependent upon the extent of obstruction; if obstruction is not complete it may be possible to aid the vascular outflow by dilators, etc., as was accomplished in one of our recent cases in which good vision resulted.

Case 2 illustrates the rapid death of the retinal elements from loss of blood supply. Although collateral circulation and return of the blood supply occurs, the retina dies early and recovery is rare in cases of central arterial embolus unless, by chance, treatment is instituted immediately and the embolus is moved along to a small vessel. This should be attempted either by aqueous drainage or by forceful massage of the globe. While the venous thrombosis is very hemorrhagic, the arterial cases rarely produce hemorrhages and then very few and slight. The prognosis is poor in Case 2 as this patient does not have a cilio-retinal vessel which might supply the macula area and keep the central vision intact. The hopeful side of these seemingly hopeless cases is that rarely is the other eye similarly affected and, occurring as it does in middle or late adult life, there is a good possibility that the patient will escape blindness.

## LUNG ABSCESS FROM ASPIRATED PEANUT WITH RECOVERY AFTER REMOVAL

### *Report of a Case*

PAUL M. MOORE, JR., M.D.

The following case is reported because it shows the very rapid recovery from a lung abscess which followed removal of the causative agent. This occurred in spite of the fact that the foreign body had been present for four weeks. This case also illustrates the danger of certain types of foreign bodies and the importance of repeating the bronchoscopic examination if the response is not at first satisfactory.

### REPORT OF CASE

The patient, a boy 5 years of age, was admitted on the medical service of Dr. John Tucker on June 24, 1938. The following history was obtained: Four weeks previously, severe cough, choking, and respiratory difficulty had developed while the child was eating peanuts. A day later, a bronchoscopic examination had been performed and a piece of peanut was removed from the right main bronchus. Within 24 hours edema and obstruction of the larynx developed and it became necessary to do a tracheotomy.

The cough persisted and had grown more severe during the preceding week. At the time of our examination it was productive of green pus. Since the onset of the illness, the temperature had been elevated in the morning and had been persistently high for the previous week. The patient had lost his appetite and refused to eat properly with a resultant loss of 9 pounds in weight. Sleep had been fitful and he had been complaining of aching in the arms and back.

The previous medical history was irrelevant except for pneumonia at the age of 6 months and measles 6 weeks before the onset of the present illness.

Examination revealed an ill child whose rectal temperature was 102.5° F., pulse rate 120, and respirations 40. The tracheotomy wound was closed in the depths but was not entirely healed at the skin surface. The pupils were equal and reacted normally to light. Examination of the nose showed the nasal septum to be somewhat irregular, the turbinates to be normal, and the middle meati clean. The teeth and tongue appeared to be normal. The tonsils were fairly large but showed no acute inflammation. The canals and drums of the ears were normal.

The expansion of the chest was good and equal. The percussion note over the right lower lobe posteriorly was flat, the breath sounds were absent, and transmission of the whispered and spoken voice showed a consolidated area in the right lower lobe. (Fig. 1.)

## LUNG ABSCESS FROM ASPIRATED PEANUT

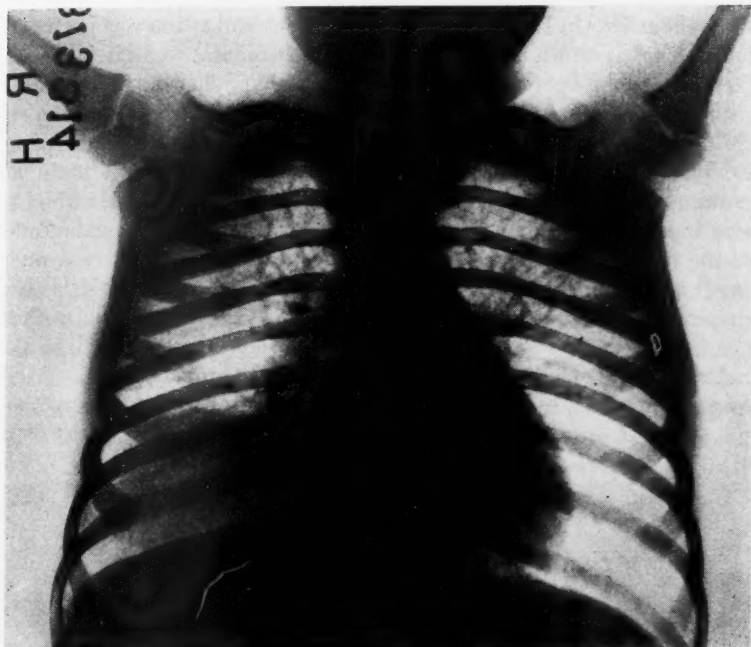


FIGURE 1: Roentgenogram showing lung abscess in lower lobe of right lung.

Examination of the blood showed 4,650,000 red cells, 15,100 white cells, and 67 per cent hemoglobin with 73 per cent neutrophils, 22 per cent lymphocytes, and 5 per cent monocytes. The blood group was two. The level of the blood sugar was 90 mg. per 100 cc. one hour fasting. The blood Wassermann and Kahn tests gave negative reactions. Examination of the urine showed a trace of albumin and 5 to 10 red blood cells per high power field; specific gravity 1.010; reaction 6.0; sugar 0. A culture of the sputum showed nonhemolytic streptococci.

A diagnosis of lung abscess was made.

I saw the patient in consultation with Dr. Tucker on the day of admission. We felt that, in all probability, a piece of peanut remained in the lung and that this was responsible for the continued suppuration. It was decided to use medical management and observe the patient for a few days before instituting further treatment. Sulfanilamide was administered, reaching a blood concentration of 18.0 mg. per 100 cc. Postural drainage and general supportive measures were employed.

During the next three days there was no improvement and the temperature ranged from 99.5 to 103.4° F. with one spike a day. Respirations

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were about 40. On June 27, a bronchoscopic examination was performed under local anesthesia. One-half grain of nembutal was given one-half hour before the operation. The mouth and hypopharynx were sprayed with a 2 per cent solution of pontocaine. With this preparation, the child cooperated beautifully and the Jackson bronchoscope was passed easily. The corina was sharp and well defined, the left main and terminal bronchi were normal. The mucosa of the right main bronchus was injected and somewhat edematous. One of the terminal bronchi of the right lower lobe showed marked swelling of the mucosa and a small stream of pus was coming from it. As this bronchus dilated on inspiration, a piece of peanut could be seen. This was grasped with the peanut forceps. Fortunately, the fragment consisted of less than half a nut and could be removed through the bronchoscope. As the foreign body came out, a large amount of foul, somewhat sanguinous pus escaped. This was aspirated very thoroughly and the tip of the

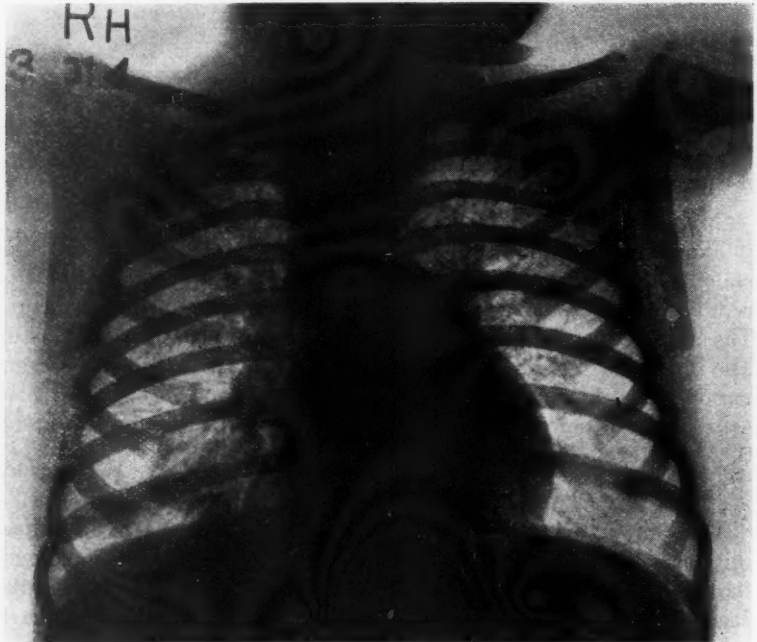


FIGURE 2: Roentgenogram showing the abscess cleared following removal of peanut.

aspirator was carried as far down into the bronchus as possible. A careful search was made for more fragments and two very small pieces were removed.



## LUNG ABSCESS FROM ASPIRATED PEANUT

The child was returned to bed in good condition and given steam inhalations of tincture of benzoin. No respiratory difficulty developed. At 4:00 o'clock in the afternoon, the temperature again rose sharply to 103.4° but it fell quite rapidly, reaching 97.6° F. at midnight. The next day the temperature remained between normal and 99.6° F. and the respirations were 40. The following day the temperature was normal and respirations dropped to 30, and then to 20 on the third day when he was discharged.

A roentgenogram of the chest taken on June 30, the day of discharge, showed less density in the area of pneumonitis.

The patient was seen again on July 14, seventeen days after operation. The temperature had remained normal, there was only a slight cough in the morning, the appetite was good, and he had gained  $3\frac{3}{4}$  pounds. There was still some impairment of resonance and distant breath sounds over the base of the right lung but a roentgenogram (Fig. 2) of the chest showed the lungs to be clear except for some old fibrous scar tissue where the abscess had been. The white blood cells numbered 5,950.

### COMMENT

The tendency for vegetable foreign bodies, especially peanuts, to produce pneumonitis and lung abscess is well known. The persistence of lung suppuration for three weeks following the removal of a piece of peanut indicated the probability that a foreign body was still present. The prompt cessation of fever and other symptoms after removal of this remaining foreign body was very gratifying.

The use of a spray of a 2 per cent solution of pontocaine in the throat in children before endoscopy is perfectly safe. It produces a local anesthesia which eliminates pain and this combined with a small dose of some sedative such as nembutal makes it possible to secure a certain amount of cooperation from the child. Most children are good patients if they are not frightened or hurt and I believe they are entitled to as much consideration as an adult.



## SUCCESSFUL RESECTION OF THE HEAD OF THE PANCREAS FOR CARCINOMA

### *Report of a Case*

GEORGE CRILE, JR., M.D.

Until 1935 when Whipple, Parsons, and Mullins<sup>1</sup> described the radical two-stage operation for carcinoma of the ampulla of Vater, the surgical treatment of carcinomas in the region of the head of the pancreas had met with consistent failure. Later, in April, 1938, Whipple<sup>2</sup> collected 11 cases in which resections of the head of the pancreas had been performed for carcinoma. One additional case<sup>3</sup> has been reported, but only six of these 12 patients have survived the operation.

In the case reported here, the patient was suffering from a carcinoma of the head of the pancreas and has made a satisfactory convalescence following radical resection of the head of the pancreas and duodenum.

### REPORT OF CASE

The patient was a man, 37 years of age, whose chief complaint was jaundice. Five months before entry, he had noticed sluggishness, nervousness, and easy fatigability. This was followed in two months by painless jaundice associated with marked pruritis. Thirty pounds in weight had been lost.

Examination showed deep jaundice, a smooth, firm enlargement of the liver extending two fingers' breadth beneath the costal margins, and a large tense rounded mass in the region of the gallbladder.

The icterus index was 100 units and the coagulation time of the blood was one hour. The blood phosphatase was 6.6 units. Roentgen examination of the duodenum showed no evidences of a tumor in the region of the ampulla of Vater. A plain film of the gallbladder region failed to demonstrate any opaque biliary calculi. There was a moderate secondary anemia, the red blood cells numbering 3,780,000 and the level of the hemoglobin being 61 per cent. The level of the blood urea was 24 mg. per 100 cc. and urinalysis was negative except for a trace of albumin, a few hyaline casts, and a great deal of bile.

A diagnosis of carcinoma of the head of the pancreas was made and exploration was advised.

The patient was given a low fat, high carbohydrate diet, 1000 cc. of a 10 per cent solution of glucose intravenously, and 10 cc. of a 10 per cent solution of calcium gluconate daily for 3 days. A transfusion of 500 cc. of whole blood was then given and the abdomen was explored under spinal anesthesia through a right rectus incision. The gall-

## SUCCESSFUL RESECTION OF HEAD OF PANCREAS FOR CARCINOMA

bladder and common duct were found to be enormously dilated. The common duct easily admitted the index finger which was passed downward, encountering a hard mass in the region of the head of the pancreas. This mass was about one and one-half inches in diameter and appeared to be movable. There were no metastases in the liver and there was no enlargement of the regional lymph nodes. The remainder of the pancreas felt tense and cystic. A cholecystogastrostomy was performed, a stoma well over an inch in diameter being made. After operation a second blood transfusion was given.

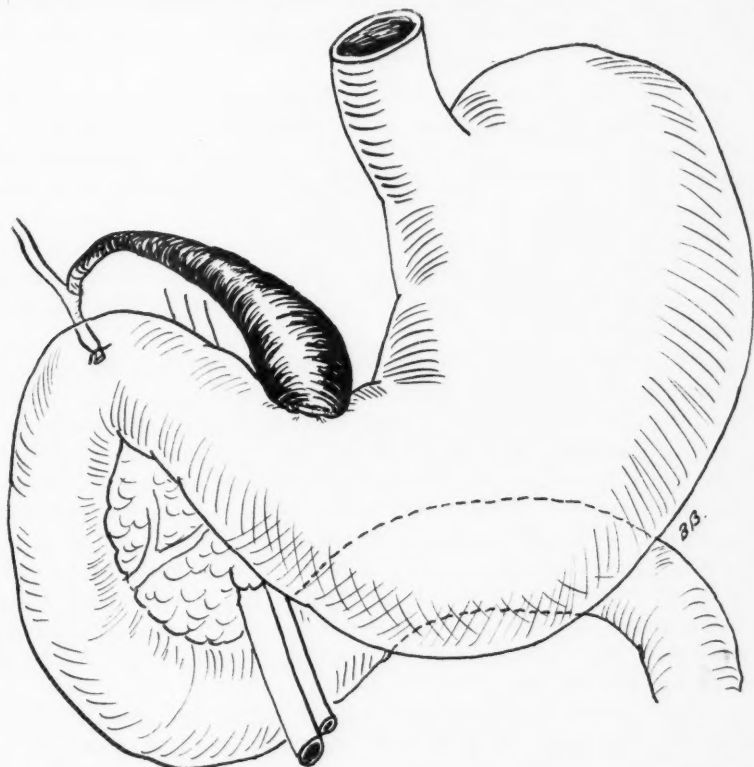


FIGURE 1: First stage of radical resection of the head of the pancreas. Figure shows common duct ligated and gallbladder anastomosed to the stomach.

Convalescence from this procedure was complicated on the second postoperative day by a secondary hemorrhage from a tiny subcutaneous blood vessel. The vessel was easily caught and tied. Two more transfusions of 500 cc. each were given. On the fourth postoperative day, the patient became very pale, the blood pressure fell to 70, and the level

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of the hemoglobin to 35 per cent. A large tarry stool was passed. Several more blood transfusions were given immediately and the following day another transfusion was given. A total of 4500 cc. of blood had been administered by the seventh postoperative day and the bleeding had apparently stopped. The bleeding and clotting time were then within normal limits and the icterus index had fallen to 30 units. From the fourteenth to the eighteenth postoperative days, there was an irregular elevation of the temperature to as high as 101.2°F. It was thought that this was the result of a mild cholangitis. The patient was discharged from the hospital and returned to his home to recuperate. He was instructed to return at the end of three weeks for removal of the head of the pancreas.

The convalescence at home was complicated for the first few weeks by a persistence of the cholangitis, the temperature rising on several occasions to 104° F. The temperature then returned to normal and the patient rapidly regained his strength and gained 10 pounds in weight. The jaundice cleared up completely.

On his return to the hospital a little more than two months after the original operation, the icterus index had fallen to 10 units and the level of the hemoglobin was 81 per cent. The bleeding and clotting time were now normal.

In view of the excellent progress that had been made, it was decided to resect the head of the pancreas. Under spinal anesthesia, a transverse abdominal incision was made and the peritoneal cavity was opened. Dissection was rendered difficult by numerous adhesions. There had been no appreciable change in the size of the tumor in the head of the pancreas or in its mobility. In order to expose the pancreas, the gastrocolic omentum was divided along the greater curvature of the stomach. The duodenum was then divided just distal to the pylorus and the proximal end was inverted with two layers of continuous catgut sutures reinforced with interrupted silk sutures. The gastroduodenal artery was ligated and the common duct was isolated and ligated with a silk tie. The duodenum was mobilized from its lateral border and was again severed, this time in its third portion and the distal end inverted. The hand could then be inserted behind the head of the pancreas which was firmly adherent to the duodenum. A finger was placed beneath the neck of the pancreas well distal to the tumor and the pancreas was cut across. The pancreatic duct was dilated to the size of the index finger and this made the entire organ feel tense and fluctuant. The cut end of the pancreas including the dilated duct was closed with three mattress sutures of alloy steel wire. Upon section of the pancreas, the portal vein was exposed at the site of its formation from the splenic and superior mesenteric veins. The head of the pancreas was dissected

## SUCCESSFUL RESECTION OF HEAD OF PANCREAS FOR CARCINOMA

from the superior mesenteric and portal veins, and the entire head of the pancreas, the duodenum, and the surrounding areolar and lymph gland bearing tissues were removed in a single block. There was some

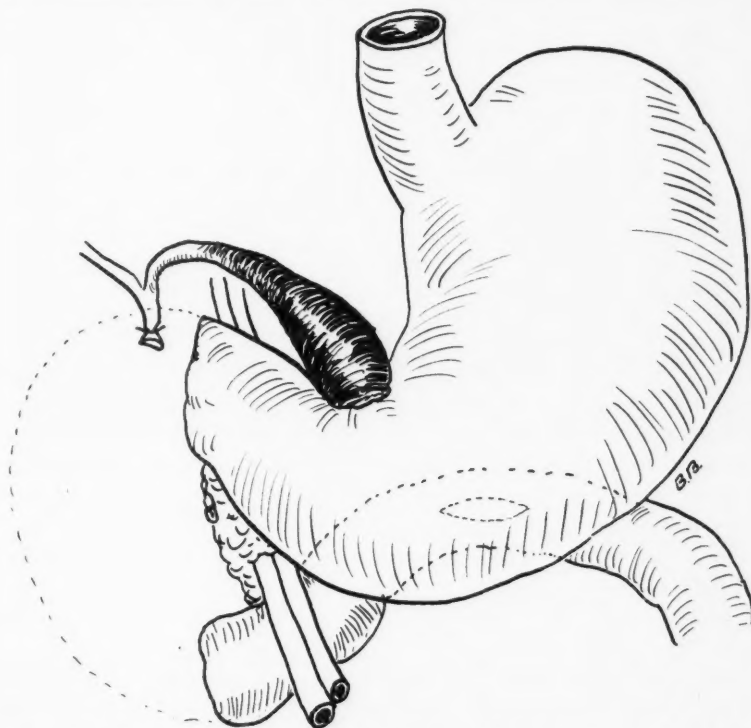


FIGURE 2: Second stage of radical resection of the head of the pancreas. Figure shows ligated common duct and cholecystogastrostomy performed at the first stage. In addition, the stomach has been severed at the pylorus and the proximal end inverted. The duodenum and head of the pancreas have been removed and the distal end of the duodenum has been inverted. A posterior gastroenterostomy has been performed.

troublesome oozing from small branches of the superior mesenteric vein which apparently entered the pancreas directly but this was easily controlled with a small amount of packing. During the course of the operation, the patient received 500 cc. of blood and 1000 cc. of 10 per cent glucose solution. The blood pressure at the close of the procedure was 100 systolic, 65 diastolic and the pulse rate was 115. Four cigarette drains were placed in the pancreatic bed and the abdomen was closed with continuous catgut sutures in the peritoneum and interrupted alloy steel wire sutures in the fascia.

On the night of the operation, the patient's temperature rose to 106°F.,

but his pulse remained of good quality and his general condition appeared to be remarkably good. By the second postoperative day, the temperature had fallen to normal but the patient then experienced a chill and the temperature again rose to 105° F. The icterus index rose to 25 units and it was thought that the febrile reaction represented a recurrence of the previous cholangitis. A blood culture, made just after a chill, was positive for *B. coli*. All the drains were removed by the fifth day. On the ninth postoperative day, bile appeared in the drainage from the wound and dye taken by mouth promptly appeared on the dressing, indicating that the fistula was in all probability from the distal end of the stomach. On the eleventh postoperative day, profuse bleeding into the fistulous tract occurred and a large hematoma formed in the abdominal wall. Several transfusions were given and the bleeding stopped spontaneously. On the fifteenth postoperative day the hematoma, which had become infected, was evacuated and the temperature and pulse rate fell to normal and remained so. A total of 3500 cc. of blood had been given at this hospitalization and the level of hemoglobin was now maintained at 70 per cent, the icterus index was 10 units, and the patient was eating well.

The fistula was quite small and drainage was easily controlled by a small amount of packing. By the thirty-second postoperative day, the fistula was nearly closed and the patient was discharged from the hospital. At the time of discharge there was no excess of fat in the stool and the digestion of the food was normal in every respect. Sugar did not appear in the urine and there was no significant alteration in the blood sugar levels.

Two months after operation, the patient is able to return to work. He has gained in strength and weight and he reports that the fistula has closed.

Examination of the specimen removed was as follows:

*Gross:* Specimen consists of the duodenum and head of the pancreas weighing 100 grams (Fig. 3). The head of the pancreas is adherent to the duodenum over an area about 4 to 5 cm. in diameter. The head of the pancreas which measures approximately 4.5 x 4 x 2.5 cm. is quite hard, indurated, and appears to be diffusely involved by a neoplastic process. Sections through the pancreas show relatively little normal pancreatic tissue but a white, somewhat granular neoplasm with considerable stroma is present. The pancreatic ducts at the site of the division of the pancreas are quite markedly dilated and thick walled. The distal end of the common duct passes through the mass and a probe cannot be passed through the duct. There is a small amount of fat around the pancreas in which there are a few lymph nodes, some of which appear to be involved by the tumor.

## SUCCESSFUL RESECTION OF HEAD OF PANCREAS FOR CARCINOMA

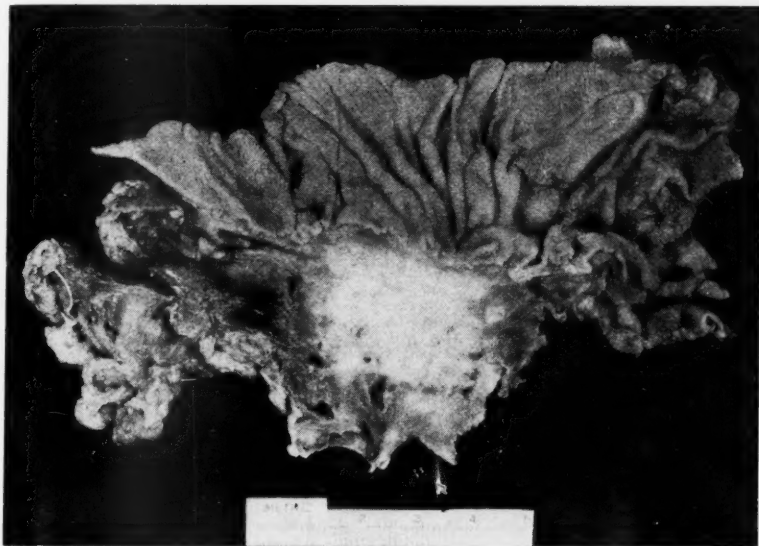


FIGURE 3: Photograph of gross specimen cut to show carcinoma in head of pancreas.

**Microscopical:** A section through the duodenum and the head of the pancreas in the region of the papilla shows an intact intestinal mucosa with a mild inflammatory reaction but no neoplastic involvement of the epithelial coat. In the head of the pancreas there is an adenocarcinomatous growth (Fig. 4) of ductal type quite well differentiated and consisting of small and large irregular spaces lined by single and multiple layers of cuboidal and columnar mucus-secreting epithelial cells with a few mitotic figures present. There is marked atrophy and fibrosis of pancreatic tissue and the tumor extends through the muscular and submucous coats of the intestine. From its histological characteristics, the tumor probably originated from the pancreatic ducts or possibly from the common bile duct but the involvement is too diffuse to determine which. A section of a lymph node shows no metastasis.

**Pathological diagnosis:** Ductal carcinoma head of pancreas.

### COMMENT

In this case the tumor was highly differentiated and was of a relatively low grade of malignancy. There was no evidence of metastasis to the regional lymph nodes and examination of the gross specimen indicated that the tumor had been completely removed. The prognosis should therefore be favorable.

Eight autopsies have been performed at the Cleveland Clinic hos-





FIGURE 4: Photomicrograph of carcinoma of head of pancreas.

pital on patients who have died following exploratory or palliative operations for carcinoma of the head of the pancreas. In six of these eight cases, the tumor was limited to the area resectable by radical oper-



## SUCCESSFUL RESECTION OF HEAD OF PANCREAS FOR CARCINOMA

ation. The autopsy studies of Rives, Romano, and Sandifer<sup>4</sup> have shown that in 10 per cent of their cases, the carcinoma had not metastasized at the time of the patient's death. In 60 per cent of their surgical cases there was no apparent metastasis at the time of operation. Ransom's<sup>5</sup> autopsy figures do not show so high an incidence of localized lesions in the head of the pancreas but indicate that primary carcinoma of the bile ducts and of the ampulla of Vater are actually more common than primary carcinomas of the head of the pancreas and that many of these tumors are localized and resectable at the time of the patient's death.

These considerations, coupled with the well known fact that a stone in the common duct can cause jaundice without pain, should influence us to give a more hopeful prognosis to patients with painless jaundice. With the recent technical advances in the surgery of the head of the pancreas, it is now possible to offer patients with carcinoma a chance for permanent cure. As surgeons develop greater skill in this field, the mortality rate will be lowered and the percentage of cures will increase. It is now clear that every patient with persistent, painless jaundice of the obstructive type should have the benefit of an exploratory operation and of resection of the tumor if it is operable.

To Whipple belongs the credit for devising the radical two-stage operation for carcinoma in the region of the ampulla of Vater and the head of the pancreas. Applying his experimental work, he demonstrated that the external secretion of the pancreas was not necessary to life or well being and simplified pancreatic surgery by advising simple ligation of the pancreatic duct rather than attempting to reimplant it into the intestinal tract. In the past, Whipple has performed the gastroenterostomy at the first stage of his operation, but in his latest publication he states that he is now planning to limit the first stage to an antecolic cholecystojejunostomy on the Roux principle. I believe that any step tending to shorten the first operation and diminish the tendency to cholangitis will be an advance. The greatest danger of the operation, as demonstrated by the case reported here, is internal hemorrhage following the first stage. When the jaundice has cleared, when the liver has regained its function, and when the bleeding and clotting time have returned to normal, the patient is in good condition to withstand an extensive operation.

The value of blood transfusion in the control of the tendency to bleed must be remembered. The continuous intravenous administration of from 4000 to 5000 cc. of 10 per cent glucose solution daily is of unquestionable value in supporting the function of the failing liver. I have seen several delirious patients with rising icterus indices and the typical syndrome of liver failure regain consciousness and return

GEORGE CRILE, JR.

to a normal state after glucose had been administered intravenously for 24 hours.

SUMMARY

1. A radical two-stage resection of the head of the pancreas and duodenum was successfully accomplished in a patient with carcinoma of the head of the pancreas.

2. In a large percentage of all patients with carcinoma in the region of the common duct, ampulla of Vater, and head of the pancreas, the tumor is localized and resectable at the time of the patient's death.

3. Recent advances in the surgery of the pancreas should encourage more radical attacks on carcinoma in this region.

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## ALLERGIC RHINITIS AND MIGRAINE

### *Report of a Case*

C. R. K. JOHNSTON, M. D.

The following case is reported to demonstrate the rôle of allergy in a case of rhinitis and migraine of long duration.

### REPORT OF CASE

The patient, a single woman, 39 years of age, came to the Clinic on June 25, 1937, for a general physical examination. She was a graduate nurse and had three major complaints: persistent nasal discharge and attacks of bronchitis which had been present for many years; sick headaches all her life, and varicose veins.

Since the age of 14 years, she had had chronic nasal symptoms which were characterized chiefly by a perennial anterior and posterior nasal discharge of yellowish-green, purulent mucus. These symptoms were more severe during cold weather, at which time she had frequent "head colds." Her nose was constantly congested and at times the discharge was watery rather than purulent. Several times every year and occurring at any season, she had an attack of bronchitis which lasted for two or three weeks. Much operative work, including a submucous resection at the age of 14, had been done in an effort to relieve these symptoms. Polypi were removed at the age of 15 and when 22 a tonsillectomy was performed. Washings of the antra were then tried for several years and finally an antrotomy on the right side was performed one year preceding her visit to the Clinic. Since that time there had been gradual improvement in the symptoms although they were still troublesome. Therapy with autogenous vaccine was tried but was discontinued because of severe reactions. It was also of significance that some brands of face powder caused her to wheeze and that she had kept a dog for several years.

The patient stated that all her life she had had "sick headaches." These were unilateral, although either side might be affected. The duration was from 5 to 48 hours and nausea and vomiting usually accompanied them. They occurred from one to three times monthly. There was a questionable association with the menstrual periods which, while regular, were scanty and had lasted only three days since a dilatation and curettage for menorrhagia four years previously. By taking "Veracolate," she noticed some decrease in the severity and frequency of the headaches. She knew that nervous tension increased them and suspected that chocolate and cream would produce them. One uncle had had similar headaches.

## C. R. K. JOHNSTON

The physical examination revealed a moderate degree of obesity, a tendency toward dryness of the skin and hair, a dull right antrum, and varicose veins in both lower extremities.

Routine laboratory investigation, including urinalysis, examination of the blood, determination of the level of the blood sugar, and complement fixation tests, gave normal findings. The basal metabolic rate was reported as plus or minus zero.

Investigation for the determination of allergens was advised because of the long history of symptoms which failed to yield to local treatment. Complete skin tests were carried out, chiefly by the intradermal method. Rather marked reactions were obtained to several inhalants, notably feathers of all kinds, dog dander, house dust, orris root, and tobacco. Chocolate produced the most significant reaction to food although a number of others, including milk and wheat, also gave reactions.

Instructions were given regarding a routine for the elimination of inhalants and foods to which reactions had occurred. Additional vitamins (A, B<sub>1</sub>, C, D, and G, twice daily) were prescribed to supplement the diet and she was advised to take one grain of thyroid daily.

The patient was next seen fourteen months later when she reported marked improvement. The purulent discharge had entirely cleared and she had no nasal symptoms of any kind, nor had she had any more colds. The headaches had almost ceased. She had suffered only two severe ones which she believed were caused either by excess nervous strain or dietary indiscretion. The patient had followed her regimen very carefully and had had no therapy other than that noted above. The thyroid had not been taken regularly. She was delighted with the result and felt that avoidance of chocolate was largely responsible for the relief of headaches and that dust and contact with her dog had caused most of her nasal symptoms. Her blood counts were rechecked at this time and showed no significant change.

## DISCUSSION

This case emphasizes the fact that mild nasal allergy is very commonly overlooked. I feel that it was the important factor in producing the patient's nasal symptoms and when removed the associated infection soon cleared up. The long history and the large amount of operative work which had been performed without producing adequate relief are strongly suggestive of allergy.

The typical migraine nature of the headaches also indicated that investigation for the determination of allergens should be carried out, especially in the light of the familial history of similar headaches in a maternal uncle.

## ALLERGIC RHINITIS AND MIGRAINE

In conclusion, it is suggested that all patients with a history of long-standing nasal symptoms, especially when an associated allergic state can be demonstrated, be given the benefit of an allergic investigation before nasal surgery is undertaken.

## CLINICAL APPLICATION OF THOROTRAST MYELOGRAPHY AND SUBSEQUENT FORCED DRAINAGE\*

### *Report of a Case*

WM. A. NOSIK, M. D.

In a high percentage of surgical lesions of the spinal cord, no changes in the bony structure are demonstrable by the ordinary methods of roentgen examination, even when the clinical findings are suggestive of a certain cord level. In the interest of an accurate preoperative diagnosis, so essential to the surgeon, it is necessary to resort to the use of certain substances which, when injected intraspinally and followed by roentgen examination, will outline the offending lesion and establish not only its location but often its character.

The radio-opaque oils, particularly lipiodol, have been favored for clinical usage, but not without certain reservations as to their adequacy as diagnostic media. It is obvious that they do not meet the requirements of the ideal intraspinal agent, namely: (1) that it should be non-toxic, (2) of sufficient atomic weight to cast a clear-cut shadow, (3) non-irritating, (4) miscible with the spinal fluid, and (5) readily eliminated (Coe, Otell and Hedley<sup>1</sup>).

Because it most nearly fulfilled the qualifications of the ideal medium, thorotrast attracted much attention, particularly since the work of Schoenfeld and Freeman<sup>2</sup>, and Twining and Rowbotham<sup>3</sup> in their application of this agent to encephalography and ventriculography with apparently good results but with evidence of meningeal irritation. In spite of the mild irritative reaction that attends the introduction of thorotrast, like any other foreign body, into the subarachnoid space and also the fact that the body is forced to dispose of the injected material through its own agencies, this substance gave such a nicety of cerebrospinal anatomical detail that it offered quite a temptation as a potential diagnostic aid. Realizing that it is desirable to remove any foreign substance which has been introduced into the body as a diagnostic aid after it has served that purpose, it occurred to the author that, because of its miscibility with cerebrospinal fluid, much of a subarachnoid injection of thorotrast could possibly be removed by using the forced drainage method suggested by Kubie and Retan<sup>4</sup>. With Mortensen, a series of experiments with dogs and monkeys was begun to test the practicability of such a procedure. These experiments are discussed in a previous publication<sup>5</sup>. It was observed at once that not only could the thorotrast be almost entirely removed but that the degree of reaction to this substance was brought to a minimum; likewise, it was felt quite likely that the drainage could be equally as effective in the elimination

\*Abstract of thesis which was awarded the William E. Lower Fellowship Thesis Prize for 1938.



## THOROTRAST MYELOGRAPHY AND SUBSEQUENT FORCED DRAINAGE

of both the thorium dioxide and the reaction in the human subject. Accordingly, the procedure was used and the theoretical considerations established in practical form.

In the case reported the basic principles were applied.

### REPORT OF CASE

The patient, a white girl of 24 years, who complained of difficulty in walking was seen at the Cleveland Clinic on March 1, 1938. The patient first became aware of slight spasticity of her legs one morning in September, 1933. She began to have pain of sharp, piercing nature, shooting from the gluteal regions to the backs of the legs. The pain gradually subsided to a mild chronic ache. Coughing, sneezing, and bending would exaggerate her discomfort. Two weeks previous to examination the old sharp pain with the spasticity of the legs recurred and progressed until the patient sought relief.

*Past Medical History:* Tonsillitis and tonsillectomy, 1930.

*Physical Examination:* The patient was a well developed and nourished white girl who walked with guarded gait. General examination revealed no evidences of pathological changes.

The pertinent neurological findings were: Bilateral hyperactive patellar reflexes, absent lower abdominals, questionable Babinski bilaterally, perception to both touch and pain decreased below the eleventh dorsal segment, moderate spasticity of the legs.

The clinical impression was that of an irritative lesion of the lower dorsal cord, possibly a ruptured nucleus pulposus.

Laboratory examinations of the blood serology, chemistry and counts gave entirely normal findings. Urinalysis presented no evidence of renal changes. Roentgenograms of the lumbar spine were negative. Lumbar puncture was done with no evidence of a block. Examination of the spinal fluid revealed 0 cells, negative Pandy reaction, negative gold sol, negative Wassermann reaction, and 30 mg. protein.

Because of the strong suspicion of a surgical lesion of the spinal cord, thorotrast myelography was advised by Dr. W. James Gardner, with whom these investigations are being continued. This was carried out on March 12, 1938, when 10 cc. of thorotrast were slowly injected into the lumbar sac with the patient reclining in a 30 degree angle. Fluoroscopic examination revealed a normal canal outline. Roentgenograms were made with the injection mass in the caudal sac (Fig. 1). This was then allowed to diffuse upward by shifting the level of the patient and films were made at the new level after observing it with the fluoroscope (Fig. 3). The roentgenograms revealed no evidence of a pathological process.

The patient was then returned to her room and a drainage needle

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inserted into the lumbar canal. An intravenous injection of 1500 cc. of 0.45 per cent hypotonic saline solution was made and the thorotrast-containing fluid collected. The drainage of the cerebrospinal fluid was markedly increased due to the decrease of the osmotic tension of the blood. A total return of 128 cc. was obtained in one hour which quantitatively contained 90 per cent of the thorotrast injected (Figs. 2, 4).<sup>\*</sup> The patient complained only of slight headache at the completion of the procedure. The following day was attended by a moderately severe headache which was controlled with ice caps and codeine.

The patient was discharged on March 15, 1938, in good condition, the neurological signs being unchanged. A recheck examination on March 31, 1938, revealed a definite improvement in the neurological picture.

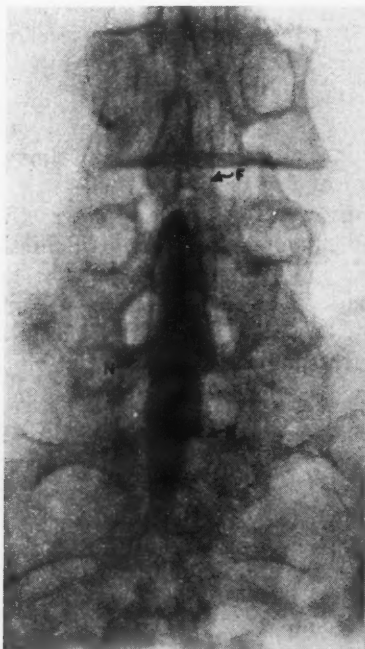


FIGURE 1: Visualization of the caudal sac with 10 cc. thorotrast. The substance had been allowed to diffuse widely before the roentgenogram was made. Fibers of the cauda equina (F) and the extension of the subarachnoid distention along the nerves are seen (N).

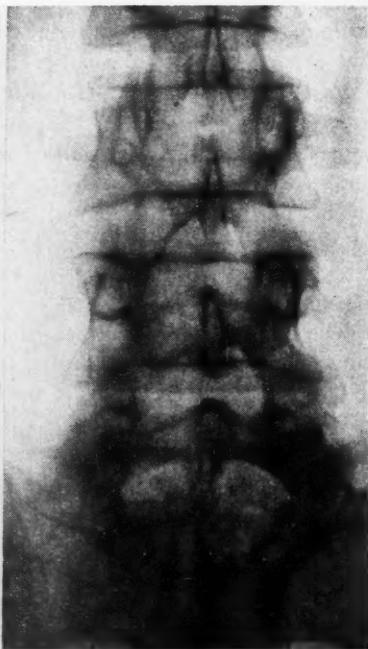


FIGURE 2: Roentgenogram made after forced spinal drainage with recovery of 90 per cent of the injected thorotrast.

*Comment:* There has been presented here a case in which thorotrast myelography was used, employing a new technic. This procedure

<sup>\*</sup> This analysis was made by Dr. D. Roy McCullagh.

### THOROTRAST MYELOGRAPHY AND SUBSEQUENT FORCED DRAINAGE

represents a combination of experimentally and clinically proved procedures, i.e., the visualization of bodily structures with thorotrast and the forced spinal drainage of Kubie and Retan<sup>4</sup>. By the use of this method it was possible to visualize the spinal canal, prove the absence of pathology of surgical nature, and remove 90 per cent of the injected radio-opaque diagnostic medium, leaving the canal free of an otherwise permanent foreign body mass. The radio-activity of the thorotrast

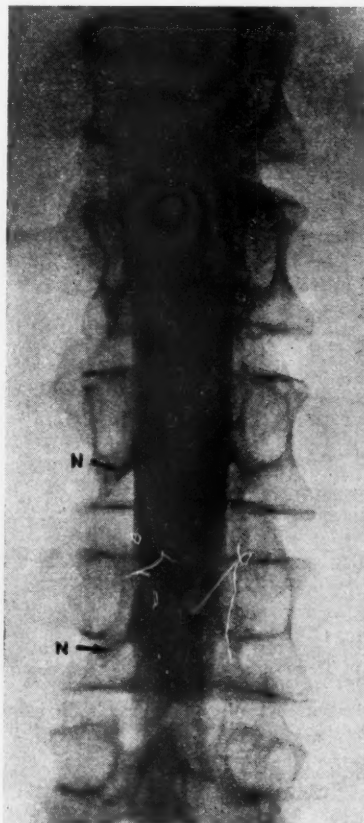


FIGURE 3: Injection-mass of 10 cc. of thorotrast taken during fluoroscopic examination of thoraco-lumbar region to demonstrate its control by gravity. N represents the perineural extension of the subarachnoid.



FIGURE 4: Roentgenogram made after drainage of subarachnoid space. The efficacy of the drainage is obvious.

dissipated in the body was calculated and found to be  $0.0108 \times 10^{-6}$  gm. radium equivalent, an amount far below that reported as the minimal toxic figure. By the use of this method the tenets of the ideal intraspinal

diagnostic agent have been upheld to a greater degree than was previously possible.

From the nature of the drainage, it is obvious that this diagnostic procedure should be applied only to cases with partial or non-obstructive lesions in the canal—the very lesions which present the greatest diagnostic problems and the most favorable surgical possibilities. With more experience, highly satisfactory myelograms and possibly even encephalograms might be made. The application of forced cerebrospinal fluid drainage to the removal of diagnostic agents of suitable physical nature is presented here.

#### CONCLUSIONS

1. A case is presented in which myelography with thorotrast and its subsequent removal by forced drainage was successfully applied.
2. One of our first applications of forced cerebrospinal fluid drainage to the removal of a diagnostic substance of suitable physical nature from the patent subarachnoidal space of man is presented here and is considered to be of basic importance.
3. A recovery of 90 per cent of the injected colloidal thorotrast was obtained after forced drainage.
4. The residual thorotrast represents a radium equivalent of  $0.0108 \times 10^{-6}$  gm., an amount far below the minimal toxic level.

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I wish to acknowledge the kind assistance and suggestions of Dr. W. James Gardner of the Neurosurgical Department whose patient is presented here, and members of the Department of Roentgenology under Dr. B. H. Nichols, namely Dr. J. C. Root and Dr. C. R. Hughes.

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## ARSPHENAMINE RESISTANT SYPHILIS

### *Report of 2 Cases*

E. W. NETHERTON, M. D.

The rapid disappearance of the cutaneous lesions of early syphilis and the *Treponema pallidum* from the exudate of moist lesions following the injection of an arsphenamine is one of the most spectacular achievements of modern therapy. The surface lesions almost invariably disappear within two or three weeks after treatment has begun and the darkfield examination usually becomes negative within twelve hours after the initial injection of a potent arsphenamine.

There are, however, rare cases in which the early lesions of syphilis do not heal following the injection of an arsphenamine. In these cases the darkfield examination remains positive even after several injections of arsphenamine. In still more rare cases, the manifestations of acute syphilis do not respond favorably to either the arsphenamines or the heavy metals. Because of this, Moore<sup>1</sup> prefers to designate this type of syphilis as treatment resistant rather than arsphenamine resistant. He states that treatment resistance occurs about once in 500 cases of patients with early syphilis.

During the past two decades numerous cases of arsphenamine resistant syphilis have been reported in the European literature and, more recently, reports of similar cases by American observers have been increasing.

Certain types of late acquired visceral syphilis and of congenital syphilis respond slowly to antisyphilitic therapy and failure to attain a complete and permanent reversal of a positive serologic test is not uncommon in acute syphilis; however, these phenomena differ from those of arsphenamine resistant early syphilis. Arsphenamine or treatment resistance is a term used to designate only that type of acute syphilis in which intensive treatment fails to remove promptly and permanently all mucocutaneous manifestations of the disease. The positive proof of resistance is the persistence of *Treponema pallidum* in the lesions in spite of arsphenamine therapy.

In treating resistant early syphilis, the lesions may enlarge and become more numerous in spite of treatment; the first injections may produce partial involution of the lesions, while subsequent injections fail to prevent their recurrence and the appearance of new lesions, or the lesions may heal during arsphenamine therapy but relapses occur when the course of heavy metal is started.

The cause of treatment resistance in early syphilis has not been determined. Most authorities feel that it is due neither to a decrease in the

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efficacy of antisyphilitic drugs, nor to the fact that the universal use of arsphenamines has produced a strain of spirochetes resistant to the drug. It is more probable that the cause of arsphenamine resistance is due to some peculiarity of the host—either the host is unable to metabolize antisyphilitic drugs or there is an alteration in the reaction of the host to the infection. There may be a disturbance in body defense mechanism of the host.

Patients with arsphenamine resistant syphilis usually do not tolerate arsphenamine as well as do other individuals and, because of this, some observers have suggested that such patients metabolize arsphenamine differently than the patients with acute syphilis in which the infection responds favorably to the drug. Moore<sup>1</sup> and his coworkers have pointed out that arsphenamine resistance and repeated infectious relapses in spite of treatment are more common in the rare cases of seronegative secondary syphilis and in secondary syphilis where relatively small amounts of reagin are present in the blood.

In arsenoresistant syphilis the eruption is frequently psoriasiform or seriginous or occurs as seborrheic papules on the face, especially on the nose and about the corners of the mouth. The scales of a psoriasiform syphilid are more oily, larger, less adherent, and of a yellowish gray color, while those of psoriasis are usually smaller, gray, imbricated, and more adherent. A squamous syphilid is more infiltrated and is frequently surrounded by a collarette of loose epithelium. This can be seen in the illustrations.

Although cases of arsphenamine or treatment resistant syphilis are rare, it is extremely important from the standpoint of public health that such cases be recognized, for the potentialities of the spread of the disease due to infectious relapses are exceedingly great. The following two cases of treatment resistant early syphilis have been observed at this Clinic during the past two years.

### REPORT OF CASES

*Case 1:* On January 5, 1937, a married man, 31 years of age, was referred to the Clinic because of a non-pruritic squamous eruption which had been present for approximately twelve weeks. The referring physician stated that, since the patient had been receiving antisyphilitic treatment from another physician but had not experienced any improvement, he had concluded that the lesions probably were those of psoriasis instead of secondary syphilis; however, he did not want to proceed with treatment without a consultation.

The past history was unimportant except that, at the age of 26, the patient had had a small penile lesion which was diagnosed by a physi-



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cian as a "hair cut." This lesion disappeared without treatment. He denied having gonorrhea or recent extramarital coitus.

*Present Illness:* The initial lesion, which was a small ulcerated papule on the prepuce, appeared about three months prior to our first examination. Within a short time, small red spots on the arms were noticed and he consulted a physician who, after finding that the serology of the blood was weakly positive (2+), instituted antisyphilitic therapy. Treatment consisted of a course of eight intravenous injections followed by three intramuscular injections. We did not ascertain what type of arsenical was used but assumed that it was neoarsphenamine. The drug was administered with a syringe and needle and at the time of each injection the patient noticed a strong ether-like odor. The initial lesions almost disappeared following the first intravenous injection but again enlarged as treatment was continued. In addition, new lesions continued to appear on the extremities and some of the older ones enlarged to form red, scaly areas. Many lesions had developed on the forehead, face, neck, and upper and lower extremities while the trunk had remained clear. There were infiltrated papules on each palm. These eruptions were limited to the genitalia and the areas just mentioned. They consisted of papules of various sizes which roughly simulated the squamous lesions of psoriasis, differing in that the scales were large, oily, and more crustaceous. The bases of the large lesions were duller red and more infiltrated than those of psoriasis. On removal of the scales, small hemorrhagic points did not appear on the surface of the papules. As can be seen in figure 1, the scales or thin crustations were thicker at the central portion of the lesions and in many instances they failed to extend to the extreme margins of the papules. Likewise, the dull red periphery of many of the papules was surrounded by a collarette of loose epithelium. There were several dull red, smooth areas of nodular infiltration on the forehead, upper lip, and chin. There were no lesions in the mouth (Fig. 2).

There was a large, moist, infiltrated papule on the prepuce just to the left of the midline. The surface of the lesion was fissured but there was no destruction of tissue such as is seen in a chancroidal infection. The regional lymph nodes were discrete and enlarged.

Darkfield examination of material obtained from the moist lesion on the prepuce was positive for *Treponema pallidum*. Both the blood Wassermann and Kahn tests gave strongly positive reactions (4+).

A diagnosis of arsphenamine resistant syphilis was made and intensive antisyphilitic treatment was recommended. The treatment was to be regular, continuous, and prolonged, and to consist of alternating courses of an arsenical and a heavy metal in accordance with the recommendations of the Cooperative Clinical Group<sup>2</sup> for the treatment of



FIGURE 1, CASE 1: Psoriasiform syphilids. Note the collarette of loose epithelium at periphery of the lesions.

early syphilis. The arsenical which had been administered (probably neoarsphenamine) was ineffective; therefore, mapharsen was selected as the arsenical to be used and the heavy metal therapy was to consist of intramuscular injections of bismuth salicylate.

On February 25, 1938, 13 months after our first examination, the

## ARSPHENAMINE RESISTANT SYPHILIS



FIGURE 2, CASE 1: Dull red, smooth cutaneous nodules on forehead. There were similar lesions on the upper lip and chin.

referring physician reported that the eruption had disappeared after a few injections of mapharsen and that there had been no mucocutaneous relapses. A recent report on the blood serology was not available, but the patient was still under treatment and was cooperating satisfactorily.

*Summary:* This patient had psoriasiform secondary syphilis which was resistant to neoarsphenamine. Lesions continued to develop even though eight treatments had been administered. A conclusive proof that the patient had an arsphenamine resistant syphilis was the demonstration at the conclusion of neoarsphenamine therapy of motile *Treponema pallidum* in the serum from the penile lesion. The infection was resistant to one member of the arsphenamine group, namely, neoarsphenamine; however, the lesions healed under mapharsen therapy.

*Case 2:* An unmarried man, 59 years of age, came to the Clinic on January 20, 1938, complaining of a non-pruritic eruption on the hands, right foot, face, and trunk.

The past history was irrelevant.

*Present Illness:* In August, 1936, seventeen months previously, the patient had sustained an injury to the right hand. This was a superficial puncture of the skin on the dorsal surface of the right hand near the base of the thumb. Within a week, the base of the wound became indurated and a serous exude could be obtained from its surface. There was no acute cellulitis. In a few days the right epitrochlear lymph gland became enlarged. He then consulted a physician who thought the indurated lesion on the hand was an extragenital chancre. A dark-field examination was made on three different occasions and at the third examination it was positive for *Treponema pallidum*.

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Antisyphilitic treatment was started and a few hours following the administration of the initial injection of neoarsphenamine a generalized pruritus developed but this disappeared the following day. Three days later, he received another injection of neoarsphenamine and that night the ankles and eyelids became edematous and the generalized pruritus was intense. The edema and itching disappeared within two days and later a third injection of neoarsphenamine produced a similar but more mild reaction. Since neoarsphenamine was not tolerated, intravenous therapy was discontinued and treatment was changed to intramuscular injections of bismuth. He had received 40 injections of bismuth since arsenical therapy has been discontinued.

A few days following the first injection of neoarsphenamine, dull red, scaly areas appeared on the tips of the middle and ring fingers of the right hand. The initial lesion on the hand gradually disappeared, but the lesions on the fingers enlarged and extended to involve the respective nail folds and nail beds, causing the nails to become friable, rough, and broken (syphilitic onychia). Practically the whole circumference of the distal half of each finger became involved by painless, non-pruritic, dull red, scaly, infiltrated plaques (Fig. 3). Several attempts had been made to find a fungus on the scales and friable nails. Roentgen therapy and topical applications failed to be beneficial. Several blood Wassermann tests had been made during the preceding year and all had been reported as negative.

The eruption remained limited to the right middle and ring fingers until October, 1937, when red spots began to appear on the dorsal surface of both hands, on the flexoral surface of the right wrist, and palm, on the palmar and lateral surfaces of the right thumb, on the right foot, the trunk, face, and neck. Recently, a large, moist, gray patch had developed on the dorsal surface of the tongue.

When this patient came under our observation, there was a large, scaly, infiltrated, dull red, irregular plaque on the dorsal surface of the right hand. It extended laterally over the ulnar surface of the hand to involve a portion of the palm. A similar but more infiltrated serpiginous plaque involved the flexoral surface of the right wrist and extended to the thenar and hypothenar portions of the palm (Fig. 4). The radial side of the right wrist and right thumb were involved by the same plaque. The right middle and ring fingers were involved by a similar eruption, particularly their distal portions. Both nails were rough and broken, and their folds were red, infiltrated, and scaly. There was no suppuration beneath the nail folds.

The infiltration was a definite characteristic of the lesions and it was especially noticeable in the lesion on the flexoral surface of the wrist.

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The scales were large, oily, and adherent. There was a collarette of loose epidermis at some portions of the periphery of each lesion.

There was a similar squamous lesion on the dorsal surface of the right foot at the base of the large toe and the one adjacent to it. The plaque also involved these toes. The soles were free of lesions.

There were large, flat, scaly papules on the back and upper extremities.



FIGURE 3, CASE 2: Large, squamous plaque on dorsal surface of the hand. Syphilitic onychia of nails of ring and middle fingers.

The scales were large, oily, and loosely adherent. Each lesion was infiltrated. There were a few dull red, smooth, cutaneous nodules on the face, there was one on the upper lip and another near the right corner of the mouth as can be seen in figure 5. There was a large, gray,

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moist patch on the dorsal surface of the tongue. There was no bismuth line on the gums and there were no signs of a bismuth stomatitis.

The blood Wassermann and Kahn tests gave strongly positive reactions (4+) and a darkfield examination of serum from the patch on the tongue was positive for *Treponema pallidum*.

A biopsy of one of the papules on the back showed a chronic inflam-



FIGURE 4, CASE 2: Infiltrated squamous plaque on wrist and palm. Note collarette of loose epithelium at margins of the lesions.

matory perivascular lymphocytic infiltration and fixed tissue proliferation in the corium which was compatible with the diagnosis of syphilis.

A diagnosis of treatment resistant early syphilis was made and treatment was begun. Since neoarsphenamine was poorly tolerated, treat-



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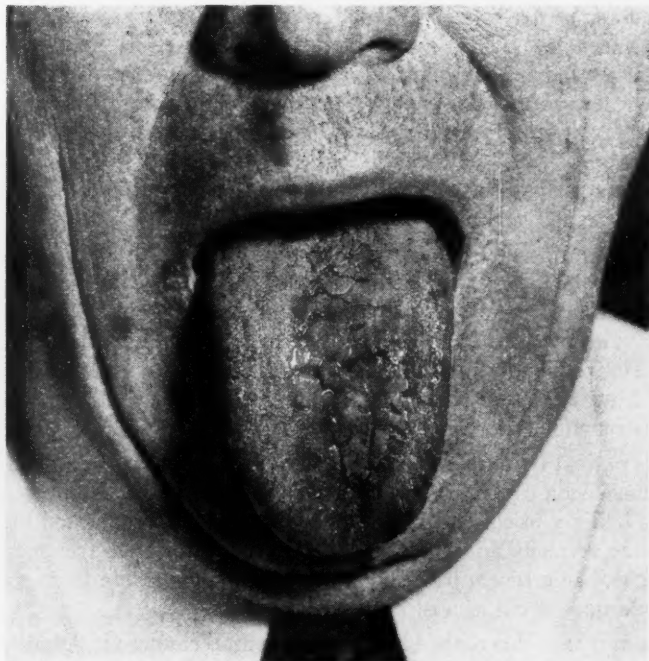


FIGURE 5, CASE 2: Large mucous patch on dorsum of tongue. Note smooth cutaneous nodule on upper lip and one near right corner of the mouth.

ment was to consist of courses of mapharsen alternating with courses of mercury. After two injections of mapharsen, a total of 0.08 gm., which were given four days apart, the infiltration in the lesions was less and the patient stated that he felt better than he had for a long while.

Treatment was continued by the patient's physician and at the end of two months the lesion on the tongue and those on the face, trunk, and arms had disappeared; however, there was still some redness and infiltration of those on the right hand and wrist. Treatment was continued with 0.06 gm. mapharsen every five days until he had taken 15 injections and then, contrary to previous recommendations, his physician advised that he take mixed treatment in the form of pills. At this time there was some redness of the lesions on the hands although infiltration was slight.

Within two weeks there was a recurrence of the infiltration in the reddened areas on the right hand and large, dull red, infiltrated plaques and papules appeared on the sole of each foot. The blood Wassermann and Kahn tests still gave strongly positive reactions. Although most of the cutaneous lesions had disappeared following fifteen injections of

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mapharsen, recurrences developed rapidly after arsenical medication was discontinued. The patient tolerated mapharsen better than neoarsphenamine, but he complained of having some nausea and of feeling listless a few hours after each treatment. Because of this he was reluctant to have further intravenous medication; however, it was obvious that treatment had so far failed to produce complete healing of the lesions and had not prevented cutaneous relapses when treatment was stopped.

Arsphenamine therapy was begun and following three injections or a total of 1.0 gm., there was marked improvement. The dose of arsphenamine was increased to 0.5 and 0.6 gm. and a total of nine injections were given. The response to arsphenamine therapy continued to be satisfactory. He frequently was troubled with nausea and vomiting two or three hours after receiving an injection of arsphenamine, but there were no serious reactions due to treatment.

This patient lives out of the city and he has continued treatment under the supervision of a physician near his home. Up to the present time he has had six injections of bismuth. He has been requested to return for more arsphenamine therapy or to arrange for such treatment near his home. In a recent letter he states, "My hands, aside from a feeling of tenderness, seem almost as good as new."

*Summary:* This patient had an extragenital chancre in August, 1936. The diagnosis was made by a darkfield examination and during the seronegative primary stage of the infection. The primary lesion disappeared following three injections of neoarsphenamine. This drug was tolerated poorly by the patient so treatment was continued with intramuscular injections of bismuth. Forty injections were given during the first 16 months of the infection. Shortly after the initial neoarsphenamine therapy and at about the time treatment with bismuth was started, a red, scaly eruption appeared on the tips of the middle and ring fingers of the right hand. These lesions enlarged until the distal half of each finger was involved. These lesions continued to persist in spite of various therapeutic procedures. During the first year, several blood Wassermann tests were reported as negative. Fourteen months later, papulosquamous psoriasiform syphilis appeared on the upper extremities, feet, trunk, face, and neck; a large mucous patch also developed on the dorsum of the tongue. *S. pallida* were found by darkfield examination of material from the lesion on the tongue and the blood serology had become strongly positive.

Bismuth therapy had failed to prevent the development of clinical and serologic manifestations of syphilis. Fifteen injections of mapharsen, most of which were 0.06 gm. each, failed to produce complete or permanent disappearance of the lesions when the interval between

## ARSPHENAMINE RESISTANT SYPHILIS

treatment was decreased to five days. Arsphenamine was effective and the lesions have not returned during the past six weeks while the patient has been receiving bismuth therapy. Further treatment and observation is necessary before the value of arsphenamine therapy can be determined. It may finally be necessary to give this patient fever therapy as an adjunct to the standard treatment procedures now being used.

### DISCUSSION

In arsphenamine resistant syphilis, the resistance is often specific for a single member of the arsphenamine group. If the resistance is to all of the arsphenamines, the lesions will heal after the administration of bismuth or mercury. Cases of early syphilis which were resistant to arsphenamine, bismuth, and mercury have been reported but they are very rare. In Case 1 the infection was resistant to neoarsphenamine but responded favorably to mapharsen and bismuth, while in Case 2, 40 injections of bismuth failed to prevent the appearance of mucocutaneous lesions and mapharsen failed to heal all the lesions and to prevent relapses when the drug was discontinued. However, the infection responded favorably to arsphenamine. In both cases the *Treponema pallidum* was demonstrated in moist lesions following the administration of standard arsenicals in amounts more than sufficient to cause the complete disappearance of the clinical manifestations in the average case of acute syphilis. The second case has not been under observation long enough to be certain that more drastic measures, such as fever therapy, will not be necessary to achieve satisfactory results.

In the management of patients with arsphenamine resistant syphilis the treatment must be intensified. The type of arsenical should be changed and if necessary the dose should be increased and the interval between treatments should be shortened. Treatment should be continuous and regular. If response to intensified treatment is satisfactory, the intensity of the therapeutic attack may be gradually decreased but treatment should be continued without rest periods until the serology of the blood and spinal fluid have become and remained permanent for at least one year. If relapses continue to occur, the use of drugs should be discontinued and fever therapy with induced malaria should be given. As soon as the fever therapy has been terminated, treatment with standard methods should again be started. Following fever therapy the lesions will usually heal promptly and relapses will not occur under treatment which previously had been ineffective.

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## URINARY EXTRAVASATION IN A NEW BORN INFANT ASSOCIATED WITH CONGENITAL STENOSIS OF THE URETHRA

### *Report of a Case*

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Congenital obstructive lesions of the urethra, though uncommon, have been recognized more frequently in recent years due to improved diagnostic methods, notably cystoscopy and intravenous urography. Most of the earlier reports were based upon autopsy findings but today the majority are recognized clinically and the various types have been reported and classified.

The present case is reported not only because it represents an unusual type of congenital urethral obstruction, but also because it was complicated by urinary extravasation.

### REPORT OF CASE

A male infant, aged three days, was admitted to the Cleveland Clinic Hospital on May 9, 1938, because he had passed no urine since birth.

The baby was a full term infant, the mother's third pregnancy. Delivery was accomplished by version extraction. The family physician reported that, although it was an unusually large baby, weighing 13 pounds and 13 ounces, no difficulty was encountered in the delivery. Examination of the baby following birth showed it to be normal in every respect. The child emitted a strong cry on being delivered and there were no signs of maldevelopment.

For the first 24 hours, the diapers were apparently somewhat moist and it was assumed that probably some urine was passing, although this is open to question. The child had passed some meconium. However, in the next 48 hours, it became evident that no urine was being passed. Twenty-four hours before admission to the Clinic there appeared for the first time some edema of the scrotum and penis. The family physician, feeling that perhaps a phimosis which was present was causing obstruction, performed a dorsal slit but this did not alter the condition. The edema extended throughout the entire perineum and scrotum and began to appear in the suprapubic region.

Physical examination revealed a rather large baby, well developed but apparently severely ill. He was not crying a great deal and gave no evidence of pain. The skin was very moist and over the entire body there seemed a peculiar redness of the skin with the exception of the hands and feet which had a dusky, almost cyanotic hue. The respirations were rapid but with adequate excursion of the lung field. The

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abdomen was not distended. Careful palpation revealed no evidence of retention of urine in the bladder.

The finding of chief interest was the presence of a marked induration which covered the entire perineum and extended up over the symphysis onto the lower part of the abdomen, extending on the left side almost to the costal margin. The scrotum, penis, and prepuce were extremely edematous and swollen. No crepitation was felt but there was marked pitting on pressure. The entire picture was rather characteristic of urinary extravasation and the condition demanded immediate attention without further study.

An attempt was made to pass a urethral catheter but both catheters and bougies met an impassable obstruction in the membranous portion of the urethra. The only alternative was to perform a suprapubic cystotomy which was advised and carried out.

At operation, the subcutaneous tissues were quite edematous and the perivesical space was infiltrated with extravasated urine. It was interesting to note that when the perivesical space was exposed and sponged, the scrotal and penile swelling showed marked regression. The bladder was found to be quite small with a distinctly thickened wall and contained only a small amount of urine. No rupture of the bladder could be demonstrated and as the child's condition did not warrant a prolonged search for the point of extravasation, a small mushroom catheter was fixed in the bladder and the perivesical space thoroughly drained. The wound was loosely closed to permit free drainage.

The condition of the baby immediately following cystotomy was quite satisfactory. On the first postoperative day some improvement was made; the child took nourishment and became somewhat brighter. The temperature during this time remained around 102° F. On the second postoperative day, the temperature came down to 100.4° F. However, on the morning of the third day, the temperature was recorded at 104.4° F. and it was noted that the skin over the entire body had a loose, shriveled appearance. On the back over the right scapular area, there was a separation of a large area of skin about three inches across. This area had the appearance of a large blister. There were numerous large reddish-pink areas on the body and extremities. Overlying these, the skin was easily slipped off and exfoliation of the epidermis soon took place at all points of pressure. The child was seen by a dermatological consultant who made a diagnosis of epidermolysis bullosa. The lips became deeply fissured. The conjunctiva were congested and there was a purulent discharge from both eyes. The lips, fingers, and toes became quite cyanotic. The child's condition grew steadily more grave and death occurred the following day.

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Permission for necropsy was granted and in this examination the points of interest were confined almost entirely to the genito-urinary tract (Figs. 1 and 2). Careful examination of all other organs showed no congenital malformations. The kidneys, ureters, bladder, and

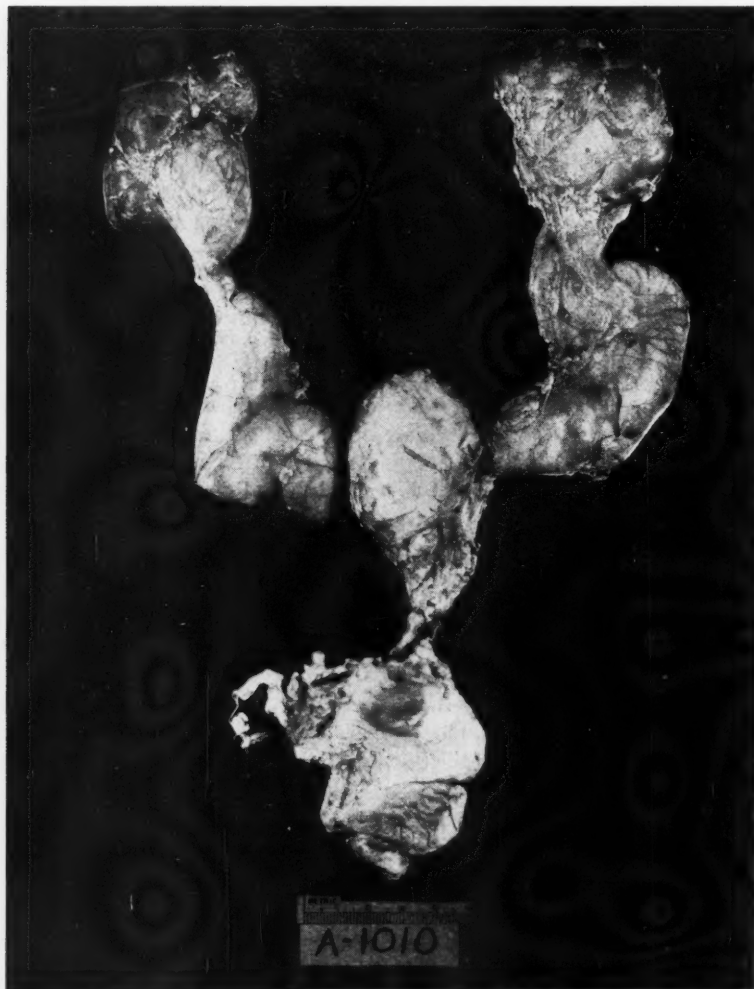


FIGURE 1: Photograph of gross specimen showing marked bilateral dilatation of kidney pelves and ureter.

urethra were examined intact and one was immediately impressed with the marked bilateral hydronephrosis and the dilated, tortuous ureters. The kidneys showed some fetal lobulation; both were about equal in



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size and on section were seen to be flattened out into a shell, the kidney tissue varying in thickness from 1 mm. to 5 or 6 mm. There was no indication of remaining pyramids, and only an occasional depression marked the position of a calix. Both ureters were enormous in size, very

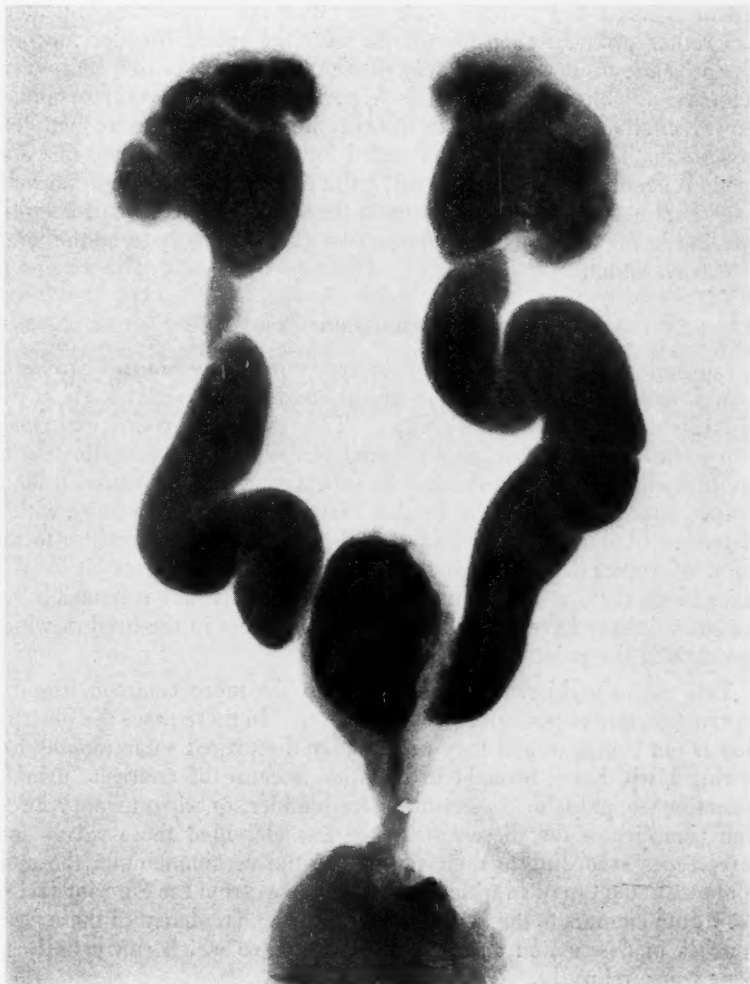


FIGURE 2: Roentgenographic outline of urinary tract after injection with contrast medium—arrow indicates point of obstruction.

tortuous, and irregular throughout their entire course. The ureters passed through the bladder wall in the usual position and manner, but at this point the lumen of each ureter was quite small compared to the

lumen elsewhere. However, a probe could be passed easily into the bladder and no obstructive lesion could be demonstrated in the lower ureter.

The bladder appeared to be about normal size for an infant but on section it was noted that the walls were uniformly thickened and there was rather pronounced trabeculation over the entire bladder mucosa. The prostatic urethra was slightly dilated but careful search showed no evidence of congenital valves or hypertrophy of the verumontanum. However, about 1 cm. distal to the verumontanum there was complete stenosis of the urethra which extended for a distance of about one and one-half centimeters. Distal to this point the urethra was again normal. Just proximal to the point of stenosis there was found a small necrotic opening in the urethra which appeared rather definitely to be the point of extravasation.

#### DISCUSSION

Congenital urethral stenosis of the type encountered in this case is of rare occurrence. It is an embryological accident and occurs as the result of faulty development of the urethra. The associated urinary extravasation makes the case even more unusual as this is a rare complication of urethral obstruction in children. In speculating as to its cause, it is, of course, conceivable that the version extraction of a large baby with a distended bladder may have increased the intravesical pressure to the point of rupture. Although this may have been a factor, it is also quite likely that the same faulty development which was responsible for the stenosis may have created a point of weakness in the urethra which determined the point of extravasation.

This case should not be confused with the more common urethral obstruction due to posterior urethral valves. In these cases the obstruction is not complete and they are usually discovered some months following birth, being brought to attention because of enuresis, urinary incontinence, palpable distention of the bladder, or when urinary infection complicates the disease. Young has classified these valves into three types according to their relation to the verumontanum, the most common being type I in which the valve passes from the anterior end of the verumontanum to the lateral urethral wall. Treatment of these cases consists in destruction or excision of the valve which can usually be done transurethraly.

The pathology in all cases of congenital urethral obstruction is quite similar. The urinary back pressure first produces dilatation of the bladder with hypertrophy of its musculature, but eventually the bladder becomes decompensated and the back pressure effect is transmitted to the ureters and kidney pelves which become enormously distended. Marked im-

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pairment of kidney function results. That this change must go on in utero is shown by our case and others reported in the literature where marked hydronephrosis existed at birth. It is believed that urinary secretion begins in the embryo at about the fifth month. Undoubtedly, serious renal impairment is present in a great many of these cases at birth; few, however, are recognizable at this time and the children live on for several years. The occurrence of disturbance of the urinary tract, most commonly infection, induces complications which require investigation. In this particular case, urinary extravasation called attention to a congenital deformity in a very young infant which necessitated immediate operative intervention.

Several methods of treatment are available. If a normal meatus is present, the passage of a bougie or filiform should first be attempted. The obstruction may be a very thin membrane and give way to gentle sounding. In so doing, however, one must exercise the greatest care in order to avoid undue urethral trauma. The second method is that carried out in this case, suprapubic cystotomy. The high position of the bladder in the infant makes cystotomy a relatively easy procedure, and where the bladder is well distended even a suprapubic puncture may be carried out. Further reconstructive procedures may then be deferred until the immediate emergency has been overcome.

## THE INVESTIGATION OF STERILITY

### *Report of a Case*

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The following case is reported in order to call attention to some of the methods which are commonly employed in the investigation of childlessness:

#### REPORT OF CASE

A young woman, 22 years of age, presented herself for examination in March, 1938. She had been married for four years, during which time contraceptives had not been used and pregnancy had not occurred. She wished to have children. The history revealed no suggestion of pituitary or hypothalamic disease except for extreme obesity. She weighed 242 pounds and her height was sixty-four and one-fourth inches. The history did not suggest the presence of hypothyroidism. The menarche had occurred at the age of 12 years and the menstrual periods had occurred regularly at about every twenty-eight days until the age of 20 when there had been amenorrhea for three months. Since that time, the menses had occurred every twenty-one to thirty-four days and lasted for six days. Mollimina were not excessive.

The texture of the skin was fine and the complexion pink. The general appearance was suggestive of Fröhlich's syndrome. Although the obesity was rather generalized, the lower legs and forearms were relatively spared.

Physical examination revealed the following findings of consequence: The thyroid gland was very slightly enlarged diffusely. The breasts were large and obese. The pulse rate varied between 60 and 80. The blood pressure was 112 systolic, 78 diastolic. Examination of the pelvis revealed no abnormality.

Urinary estrogens were measured on March 23, which was two weeks following a menstrual period. This was done by modification of the Koch method and showed more than 40 rat units in a twenty-four hour specimen of urine which is well within the normal range.

A vaginal smear was made on April 29, the preceding menstrual period having occurred on the thirteenth of the month. The vaginal smear did not show an entirely clear smear of nucleated epithelial and cornified epithelial cells. There were many leukocytes and next in order of abundance were flat, clear epithelial cells with pyknotic nuclei. This is the type of smear which is seen in castrates before a complete response to estrogenic hormone is reached and it is consistent with the pre-ovulation and the post-ovulation periods in normal women.<sup>1</sup>

Lipiodol was injected into the uterus and roentgenograms were taken immediately. These showed the oil to fill both fallopian tubes to the

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fimbriated ends, but no oil was seen in the peritoneal cavity. A roentgenogram of the pelvis was repeated six days later and this showed clearly that lipiodol had entered the peritoneal cavity, proving that at least one of the tubes was patent.

Two estimations of the basal metabolic rate averaged minus 11 per cent. The level of blood sugar was normal. The blood Wassermann and Kahn tests gave negative reactions. Examination of the blood showed 4,700,000 red cells, 5,600 white cells, 71 per cent hemoglobin, 63 per cent neutrophils, 2 per cent eosinophils, and 35 per cent lymphocytes.

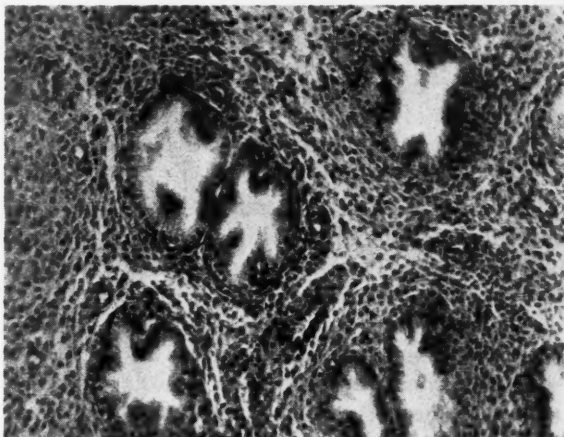


FIGURE 1: Photomicrograph of endometrial biopsy. Note the enlarged glands, their irregular infolded margins, the secretion in their lumina, and the cellularity of the stroma. (x 125).

On May 9 an endometrial biopsy was done (Fig. 1). This usually is easily accomplished in the office by means of a Novak suction curette. The endometrium in this case showed a typical premenstrual endometrium with enlarged, irregular glands containing secretory material and lying in a fairly cellular interglandular stroma. From the tortuosity of the glands, their involuted margins seen on transverse section, and their secretion, it was judged that the progesterone effect had taken place normally. Such a picture is considered good presumptive evidence that ovulation has occurred.

The patient was examined one hour after coitus and in the cervical mucus a moderate number of active sperms were found.

The husband's physical examination showed no relevant findings.

A specimen of semen was collected in a glass container. The volume was 2.5 cc. and the motility 2 plus (normal 3 to 4 plus). The count of killed sperms was 186,000,000 per cubic centimeter, a total of 465,000,-

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000. A study of stained smears of the sperms showed about 62 per cent to be morphologically abnormal. The upper limit of abnormal forms without diminution of fertility is probably about 20 per cent.

The treatment prescribed for the wife on April 29, 1938, was a diet of 800 calories per day containing 70 grams of protein; crystalline vitamin B, 5 mg. per day; calcium gluconate 1 gram daily; and ferrous sulphate for the anemia.

For the husband, wheat germ oil was prescribed in doses of 20 minims per day. A subsequent examination of the semen was done in September. The volume was 3.2 cc. and number of sperms per cubic centimeter was 49,500,000, a total of 158,400,000. The most interesting finding was the reduction of morphologically abnormal forms to 19 per cent.

On July 27, the patient's weight was 228 pounds, a loss of 14 pounds. She reported that the menstrual period due on June 6 had not occurred. Symptoms and signs of early pregnancy were present and a Friedman test gave a strongly positive reaction. On September 15, the pregnancy was still advancing normally.

### COMMENT

In the investigation of childlessness both partners should be examined to determine their general health, special attention being given to endocrine or metabolic disorders. By these methods, one may gain information regarding the occurrence of ovulation, the patency of the tubes, and the health of the endometrium. It can be shown that the sperms reach the cervical canal and live there. In the female additional information of value may be gained by studying the amount of gonadotropic and estrogenic hormones excreted in the urine and the vaginal response to estrogens in the body. Diseases of the vagina or cervix may require treatment. In the male, in addition to evidence of the state of the general health, disease of the pituitary, thyroid, or gonads must be considered. A careful study of the semen is essential. In this may be included a measure of the pH, the total volume, a careful and accurate count of killed sperms, and examination of stained smears for morphology, as well as a calculation of the degree of motility. In addition, the viability of the sperms is usually measured by repeated examinations, keeping the semen at room temperature. The epithelial debris and the number of leukocytes are also studied, and in some instances culture of the semen may be of value.

It is usually difficult to state that treatment has produced fertility, but when pregnancy occurs promptly, it is highly suggestive that some of the parts of investigation, such as tubal injection or the treatment, have been effective.

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## INFECTIONS OF THE URINARY TRACT

### *Report of a Case*

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Mandelic acid and sulfanilamide have proved to be valuable adjuncts in our armamentarium for the treatment of infections of the urinary tract. The classification of the causative organism followed by treatment with the proper drug is of the utmost importance. Not wholly without danger in administration, close supervision during treatment is recommended and certain precautions must be taken if satisfactory results are to be obtained. The following case illustrates the principles that should be followed in the use of these drugs.

### REPORT OF CASE

A nurse, 37 years of age, entered the Clinic on May 8, 1938, complaining of "pus in the urine," frequency, urgency, and pain in the right side.

In 1932 she had experienced an attack of pyelitis and cystitis which subsided in one month after the use of various urinary antiseptics. Since that time she had not been entirely free from frequency and urgency. Once or twice yearly an acute exacerbation occurred, incapacitating her for three or four weeks. In 1934 a severe attack of renal colic on the right side lasted several hours. A cystoscopic examination had been performed at that time and she was told an infection was present in the right kidney. Following this, she had taken various medications but the urine was never free from pus.

The attack which caused her to come to the Clinic began four days before admission and was manifested by pronounced frequency, urgency, dysuria, and nocturia. Slight discomfort was noted in the region of each kidney. Although she felt chilly at times, no definite chills were experienced. An examination of the urine had been made and the report was that it was loaded with pus and a few red blood cells were present.

In 1913 an appendectomy had been performed, and in 1918 a diagnosis of pleurisy had been made. For years prior to 1928, frequent attacks of tonsillitis had incapacitated the patient, so a tonsillectomy had been performed.

*Physical examination* revealed a well developed and nourished woman whose temperature was 98.6° F., pulse rate 90, blood pressure 120 systolic, 80 diastolic. No abnormal findings were noted except a small adenoma of the thyroid and tenderness on deep palpation over the kid-

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neys. Moderate discomfort was elicited by percussion in the region of the costovertebral angles.

*Laboratory findings:* Examination of the blood showed 4,970,000 red cells, 9,700 white cells, and 92 per cent hemoglobin. The level of the blood sugar was 124 mg., and of the blood urea 33 mg. per 100 cc. The Wassermann test gave a negative reaction. The basal metabolic rate was minus 14 per cent.

A roentgenogram revealed the chest to be normal. The report of the initial roentgenogram of the abdomen was: The lumbosacral region is normal. There are no suspicious shadows in the urinary tract. The kidneys are normal in size, shape, and position. There is a small calcified area in the region of the urinary bladder.

Following a cystoscopic examination, the following report was given: The cystoscope was introduced without difficulty. The patient's bladder was quite irritable and the examination was somewhat painful to her. Urine extracted from the bladder appeared quite cloudy. The bladder capacity was limited and only 100 cc. of solution could be introduced before she complained of considerable pain. Examination of the bladder revealed it to be diffusely inflamed and small petechial hemorrhages were scattered over the bladder wall. There was considerable edema about both ureteral orifices. Catheters were passed unobstructed to both kidney pelves and specimens of urine which were collected appeared slightly cloudy. The catheters were left in situ as the cystoscope was removed. Five cc. of indigo carmine was injected intravenously; it appeared from the right kidney in 3½ minutes with 4 plus concentration and from the left kidney in 3 minutes with 4 plus concentration.

A bilateral pyelogram revealed normal kidneys with the exception of a duplex pelvis on the left side.

Examination of the specimens of urine secured by catheterization revealed:

1. Bladder urine: pH 6.5, loaded with pus cells, few red blood cells; stained smear of the sediment showed gram negative bacilli, and the culture revealed *Escherichia coli*.

2. Right kidney: pH 6.5, numerous pus cells, occasional red blood cells, stained smear of the sediment showed gram negative bacilli, and the culture revealed *Escherichia coli*.

3. Left kidney: pH 6.5, numerous pus cells, few red blood cells; stained smear of sediment showed gram negative bacilli and again the culture demonstrated *Escherichia coli* as the offending organism.

*Diagnoses* were: bilateral pyelitis due to the *Escherichia coli* and cystitis due to the same organism; adenoma of the thyroid; calcified ovary.

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*Progress and treatment:* The patient was sent to the hospital and told to remain in bed. A simple bland diet was prescribed and the fluid intake was limited to 1000 cc. daily. Therapy with mandelic acid was instituted and although it increased the discomfort in the bladder for a few days, this was controlled by opium and belladonna suppositories. Twelve grams of the medication were administered daily, three grams being taken after each meal and at bedtime. A careful check of the pH of the urine revealed that it was maintained at 5.3; therefore additional acidifying agents were not required. The patient responded well to treatment and in eight days culture of the urine from the bladder showed it to be sterile. The patient was dismissed from the hospital after a period of 10 days.

One month later while at home, a second course of mandelic acid was prescribed. The patient states that she is completely relieved from symptoms and culture of the urine has showed it to remain sterile.

### DISCUSSION

In recent years two new chemotherapeutic agents have been added to our armamentarium in the treatment of infections of the urinary tract, namely, mandelic acid and sulfanilamide. The introduction of these drugs has stimulated more careful bacteriological study of the offending organisms in these conditions and more scientific approach to their eradication.

### MANDELIC ACID

The introduction of the ketogenic diet by Clark<sup>1</sup> and Helmholtz<sup>2</sup> was a distinct advance in the treatment of infections of the urinary tract. Its administration frequently caused general and gastro-intestinal symptoms which rendered it objectionable to some patients. By its employment, however, infections associated with stasis which previously did not respond to other types of medication could be treated successfully.

Fuller<sup>3</sup> later demonstrated that the bacteriostatic factor in the urine of patients on the ketogenic diet was Beta hydroxybutyric acid. When, however, this was administered by mouth, it did not prove effective as it was completely oxidized. Previously, Schotten<sup>4</sup> and Knoop<sup>5</sup> had demonstrated that mandelic acid when taken by mouth was excreted unaltered in the urine. Rosenheim<sup>6</sup> showed that it was excreted in the urine by the kidneys in a concentration adequate for bactericidal action when the pH of the urine was sufficiently low. In 1935 he reported the results secured in a series of 12 patients with infections of the urinary tract. He stated that while the series was too small to draw definite conclusions, the results merited further and extensive trial.

Since this time, numerous publications have attested to the value of this drug and it has been demonstrated that in from 80 to 90 per cent of

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uncomplicated cases of infections of the urinary tract the urine will be found bactericidal.

The institution of therapy with mandelic acid is indicated in the subacute and chronic infections, although I have employed it in the more acute stages of pyelitis and cystitis when extreme irritability of the bladder was not present. The organisms which have responded to treatment are *Escherichia coli*, *Aerobacter aerogenes*, *Streptococcus faecalis*, members of the genera *Salmonella*, *Pseudomonas* and *Shigella*. I have found that coccal infections, with the exception of *Streptococcus faecalis*, have been resistant to treatment with mandelic acid. Members of the genus *Proteus* likewise have not responded to mandelic acid therapy.

The drug most commonly prescribed is the ammonium salt in the form of the elixir or the syrup. As the percentage of the salt in the elixir and the syrup may be different, depending upon the type used, obviously the dosage of the drug must be varied. The elixir contains approximately 28 per cent of the salt and is administered in three fluid drachms (12 cc.) after meals and at bedtime. Approximately 12 gm. of the pure acid are required daily for satisfactory end results.

The pH of the urine must be maintained between 5.3 and 5.5. In the majority of cases, the mandelic acid reduces the pH of the urine to this level. If not, it may be accomplished by the use of ammonium nitrate or ammonium chloride. In addition, to increase the concentration of the drug in the urine, the fluid intake must be restricted to 1000 or 1200 cc. daily. The majority of bacilli in the urine are killed with a concentration of 0.5 per cent solution of mandelic acid in the urine at a pH of 5.5. If necessary, the concentration of the drug in the urine may be increased. As the mandelic acid is eliminated almost entirely in the urine, by knowing the 24 hour output of urine and the daily dosage we may increase the concentration to 0.9 or 1 per cent.

A simple bland diet is prescribed and if the infection is pronounced, the patient is told to go to bed.

Miscellaneous supportive measures are administered as necessary, relief of the bladder discomfort being secured by opium and belladonna suppositories or the use of the various barbiturates.

This medication is continued from ten days to two weeks unless complications arise which render its withdrawal advisable. If the urine is not sterile at this time, treatment with mandelic acid is discontinued for ten days or two weeks as the organism may have built up a resistance to the drug. Following this, a second course of treatment may be necessary to render the urine sterile.

Failure to secure good results may be due to several causes. If the organism has the power of splitting urea with the resultant formation of

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ammonia, it may be impossible to reduce the pH of the urine to 5.3 or 5.5. The patient may not tolerate the medication or, due to poor renal function, sufficient concentration of the mandelic acid in the urine may not be attained. The presence of chronic prostatitis which continues to reinfect the bladder may be conducive to securing an unsatisfactory result.

The presence of calculi, tumors, or foreign bodies as a nephrectomy tube may render sterilization of the urine difficult and finally, as stated by Braasch<sup>7</sup>, the presence of pyelonephritis with cicatricial changes in the pelvis and calices and residual urine may render a cure extremely difficult.

In patients whose renal function is not normal, careful observations should be made to avoid acidosis and similarly in children acidosis may occur unless due care is exercised in the administration of the drug. Elevation of temperature, although not pronounced, frequently occurs even in patients with normal kidneys.

Nausea and diarrhea may be present in a small percentage of cases but is not usually sufficiently pronounced to be very distressing.

In conclusion, the oral administration of mandelic acid will be efficacious in eradicating approximately 85 to 90 per cent of uncomplicated infections of the kidney and bladder. This does not infer that complete study of the urinary tract is not necessary, as coexisting pathology may be present which may ultimately destroy the kidney unless detected early and thus be responsible for failure in the use of this drug.

### SULFANILAMIDE

The second drug, sulfanilamide, was introduced by Domagk<sup>8</sup> in 1935 and used first in the United States by Long and Bliss<sup>9</sup>. Sulfanilamide administered by mouth is eliminated in the urine in the free state and the conjugated form, para-acetylamino-benzene-sulfonamide.

It is estimated that in a period of two or three days an equilibrium is established between the amount ingested and the amount excreted.

Sulfanilamide therapy has distinct advantages over mandelic acid:

1. Less distress follows its use than when mandelic acid is employed.
2. It exerts a bactericidal effect in alkaline urine. This is a distinct advantage over mandelic acid which exerts its best effect in strongly acid urine. Sulfanilamide can therefore be used in the presence of organisms which have the power of splitting urea with the resultant formation of ammonia, which renders the urine strongly alkaline.

The results, however, in eradicating the various strains of the *Proteus* group have not been as satisfactory in my hands as those of other authors.

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Sulfanilamide will eliminate between 85 to 90 per cent of uncomplicated infections of the urinary tract. In cases associated with chronic prostatitis which reinfects the bladder, striking results are frequently observed. In the coccal group of infections, however, our results have not been so striking.

The dosage advocated varies with various observers. In treating urinary infections in adults, some authors report excellent end results by the use of 60 gr. (4 gm.) daily, 15 gr. being taken after each meal and at bedtime for a period of three days, then a total dosage of 40 gr. (2.65 gm.) daily for two days, and a maintenance total dosage of 30 to 40 gr. (2 gm. - 2.65 gm.) daily for a total period of 10 to 14 days. In children, the dosage is proportionally smaller. In infants, 5 to 10 gr. are given daily; from 2 to 5 years, 15 gr. daily; from 5 to 10 years, 15 to 20 gr. daily; and over 15 years to young adults, 20 to 25 gr. daily.

There is evidence that better results may be secured when the drug is administered at regular intervals day and night. In this manner it is possible to maintain a constant free sulfanilamide level in the blood of approximately 10 mg. per 100 cc. In one of our cases of septicemia this level rose to 17 mg. per 100 cc. without producing any deleterious effects. If the drug is prescribed at regular intervals, one-sixth of the total calculated dose should be administered every four hours. I have followed this method of treatment in the majority of cases of infections of the urinary tract, administering from 15 to 20 gr. every four hours with equal amounts of sodium bicarbonate.

Sulfanilamide is an acid substance and should be administered with corresponding doses of sodium bicarbonate in order to avoid producing an acidosis and likewise to minimize gastro-intestinal symptoms.

Fluids should not be restricted when this medication is prescribed; rather, an abundant amount of water should be taken as the drug is excreted in the urine and, since it has definite toxic effects, it is essential to maintain a free rate of excretion.

In patients with poor renal function extreme care should be exercised in the administration of this drug, for if impaired renal function is present the patient may not be able to excrete concentrations in the urine greater than 30 to 40 mg. per 100 cc. That a toxic influence is exerted upon the kidney is indicated by the elevation of the blood urea and lowering of the output of phenolsulphonphthalein. In the normal kidney, however, we have seen no permanent impairment of renal function following the use of sulfanilamide.

Various manifestations of toxemia may develop, namely, cyanosis, nausea, drowsiness, tinnitus, and headaches. These are not, however, an indication to discontinue the use of the drug.



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Coggeshall and Bauer<sup>10</sup> noted no hemolytic anemias in their series. In six cases moderate to pronounced reduction in the number of red cells occurred. Four of these patients had a spontaneous reticulocytosis and a smear revealed marked macrocytosis. These anemias disappeared, however, without special treatment. In two cases, the leukocyte count fell to 1800 - 2800 two weeks after discontinuance of the drug, but again returned to normal.

Sulfhemoglobinemia, agranulocytosis, hemolytic anemia, and methemoglobinemia have similarly been reported. Careful check of the sulfanilamide content of the blood, however, and repeated blood studies minimize the development of such complications.

When prescribing sulfanilamide, saline cathartics and laxatives should not be prescribed.

Unsatisfactory results may be due to:

- (1) The patient is unable to tolerate the drug.
- (2) Poor renal function may prevent adequate excretion of the drug.
- (3) Coexisting pathology such as tumors, calculi, and foreign bodies.
- (4) Gross changes in the kidney with residual urine do not give as satisfactory results as in the normal organs.

In view of its less evident action in the presence of the coccal group, it is advisable to try neoarsphenamine when these organisms are the offending bacteria.

### SUMMARY

1. Mandelic acid and sulfanilamide are valuable drugs in the treatment of infections of the urinary tract.
2. Careful classification of the bacteria is advisable to determine which drug should be administered.
3. A more scientific approach to the eradication of urinary infections has followed the introduction of these drugs.
4. In patients who do not respond promptly to treatment, complete examination of the urinary tract is advisable to rule out coexisting pathological lesions in the genito-urinary tract.

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## TREATMENT OF UNUNITED FRACTURES OF THE NECK OF THE FEMUR

### *Report of Two Cases*

JAMES A. DICKSON, M.D.

I have previously reported our experience and the results we have secured in the treatment of fresh fractures of the neck of the femur, pointing out the advantages of the use of the Smith-Petersen nail<sup>1</sup>. At this time I wish to draw attention to two cases of nonunion of the neck of the femur treated by means of bone grafts and the Smith-Petersen nail because they exemplify the excellent results that can be anticipated from this method.

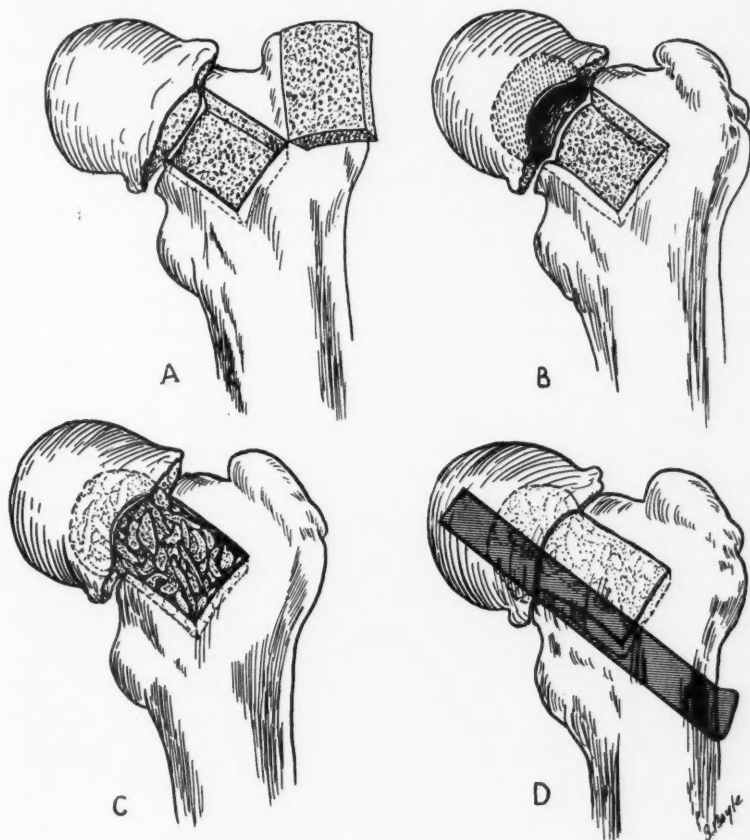


FIGURE 1: A, B, C and D: Drawings showing steps in operation by use of grafts of bone chips and Smith-Petersen nail.

## JAMES A. DICKSON

The following is a brief resumé of the operation that was used in these two cases.

The neck of the femur was exposed by the usual Smith-Petersen incision, the fracture was explored, and any necessary improvement in position was carried out. A window was made in the front of the neck of the femur (Fig. 1A) to facilitate the curettement and removal of all the scar and fibrous tissue from the fractured ends of the bone. This curettement was carried up into the head of the bone (Fig. 1B). Through this window, the cavity so formed was thoroughly packed with bone chips procured from the tibia or the crest of the ilium (Fig. 1C) and the window was replaced. A guide wire was then inserted as in an acute fracture and when a satisfactory position was obtained and confirmed by roentgen examination, a Smith-Petersen nail was driven over the guide wire and the fracture thoroughly impacted (Fig. 1D).

The results have been so gratifying that I feel confident that the use of grafts and fixation with the three flanged nail are going to be of great value in the treatment of these fractures which have proved so disappointing in the past when only medullary grafts were used.

### REPORT OF CASES

*Case 1:* The patient was a woman, 65 years of age, who in April, 1936, received a central fracture of the neck of the left femur. This was treated by means of a Steinmann pin through the lower end of the left femur and traction which was continued for a period of twelve weeks. Union did not take place and when she came under my care May 9, 1938, she was having a great deal of pain and the fracture had not united (Fig. 2).

On June 1, 1938, more than two years after the time of the original fracture, the open reduction was carried out. Under avertin and gas anesthesia, the hip joint was exposed, using the Smith-Petersen approach. The surfaces of the fracture were then freshened, removing all the old scar tissue and the cavity was packed with bone chips according to the technic described previously. The fragments were nailed into position and impacted with a Smith-Petersen pin.

The postoperative treatment was practically the same as is used in the management of acute central fractures of the neck of the femur except that this patient was given a longer period of bed rest before weight bearing was permitted. She was not allowed up in her walker until after the eighth week.

Figure 3 shows firm, bony union at the end of twelve weeks.

*Case 2:* This patient, a woman 66 years of age, received a comminuted intertrochanter fracture of the neck of the left femur in November, 1936. She was first treated in a cast, and roentgenograms taken

TREATMENT OF UNUNITED FRACTURES OF THE NECK OF THE FEMUR

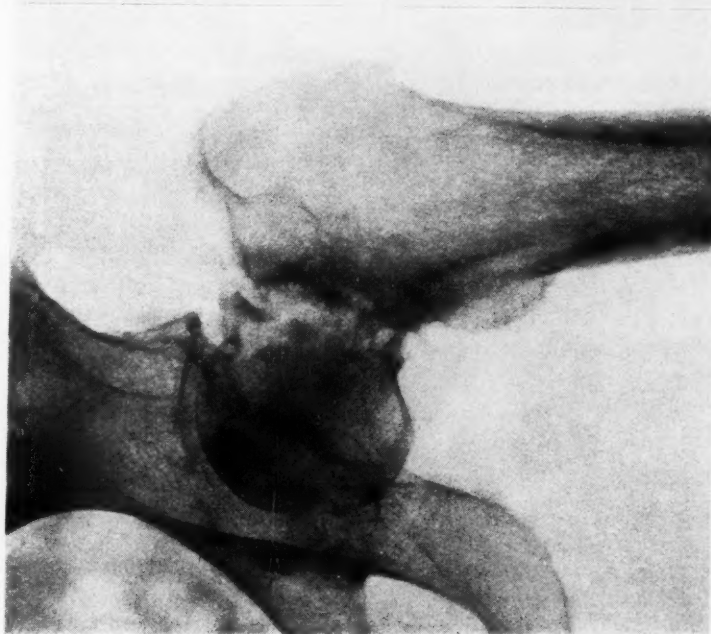


FIGURE 2: Case 1. Roentgenogram showing ununited fracture before operation.

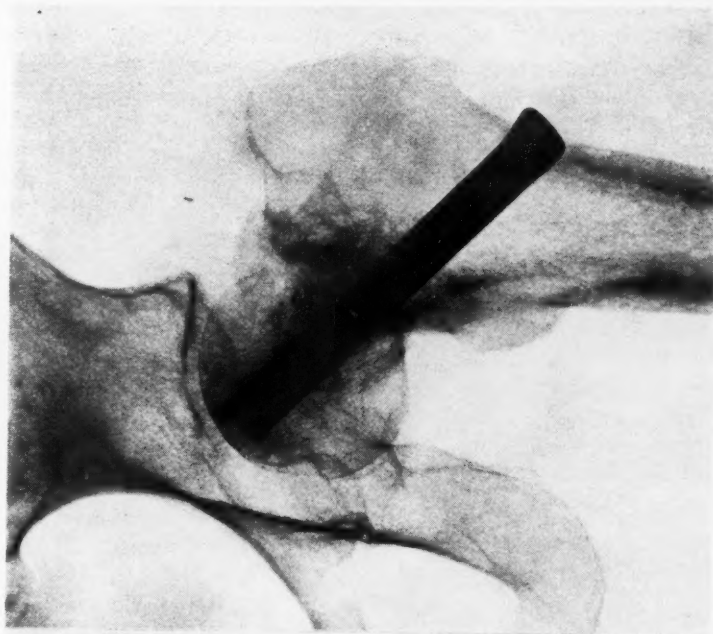


FIGURE 3: Case 1. Roentgenogram showing result 12 weeks after operation.

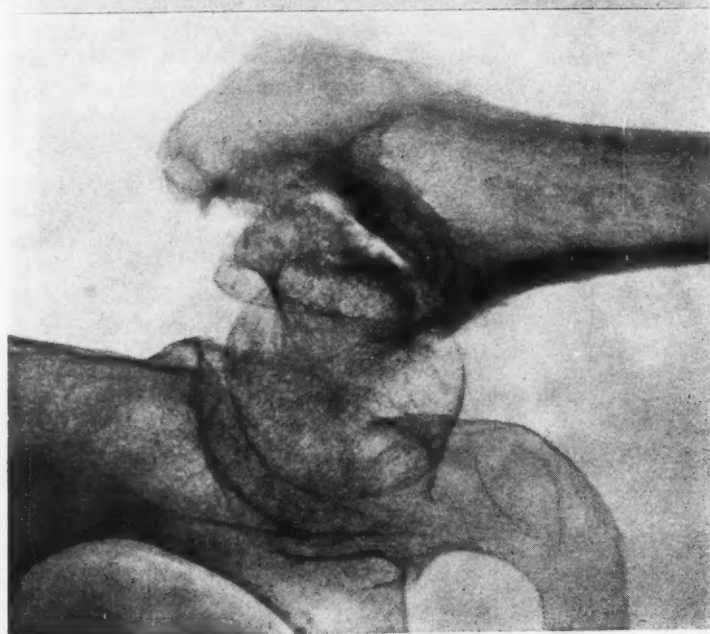


FIGURE 4: Case 2. Roentgenogram showing ununited fracture before operation.

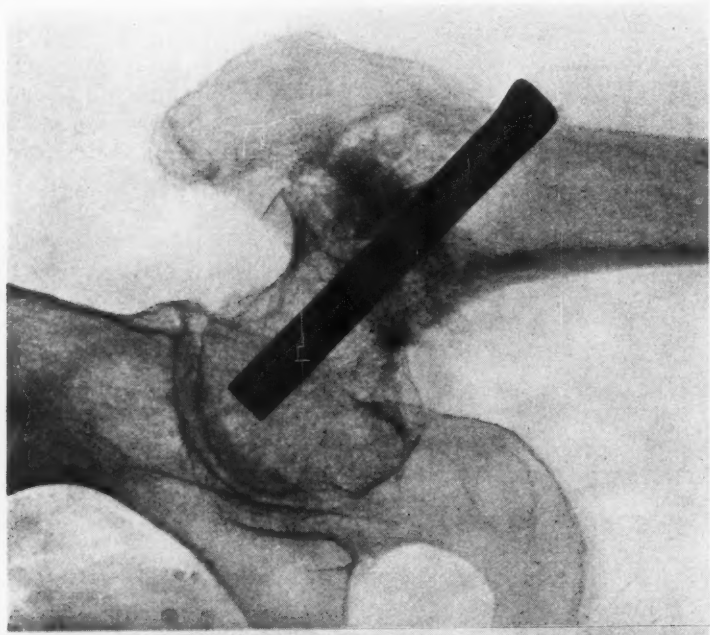


FIGURE 5: Case 2. Roentgenogram showing result 12 weeks after operation.



## TREATMENT OF UNUNITED FRACTURES OF THE NECK OF THE FEMUR

at that time showed that fairly satisfactory reduction was obtained. The cast was kept on for twelve weeks after which she wore a Thomas walking caliper. Ultimately, however, a marked coxa vara with nonunion developed. The nonunion persisted and when she came under my care on April 9, 1938—18 months after the fracture had occurred—there was considerable backward angulation and displacement at the site of the fracture, with nonunion (Fig. 4).

On June 2, under avertin and gas anesthesia, an open operation for reduction of the fracture was carried out. The surface of the fracture were freshened, bone chips were inserted, and the fracture was secured by means of a Smith-Petersen nail. Due to the fact that this was an intertrochanteric fracture it was felt advisable to give the added protection of a cast. Convalescence was uneventful.

Figure 5 shows the result at the end of twelve weeks. The fracture is well healed with excellent bony union and good position.

### COMMENT

These two cases demonstrate the possibilities in the treatment of ununited fractures of the neck of the femur. A most important factor is the early recognition of a developing nonunion as better results can be secured in cases in which operation is performed before extensive atrophy of the bone has occurred. In cases suitable for this treatment it is obvious that the end results would be much superior to the various reconstruction operations that have been used in the past. I feel confident that if this procedure were used in those cases where it is evident that nonunion is developing, much time, pain, and disability might be saved the patient. In the cases shown, it is apparent that at least a year to a year and a half of disability might have been saved these patients if operation had been performed earlier. This type of operation, preferably done early in a beginning nonunion, will also lessen the number of reconstruction operative procedures necessary to obtain stable functioning hips.

### REFERENCE

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# **The Frank E. Bunts Institute**

The Frank E. Bunts Institute will present a course in General Diagnosis and Treatment on Monday, Tuesday, and Wednesday, November 7, 8, and 9, 1938.

The program of the course and an application blank will be found on succeeding pages of this Quarterly.

## **PROGRAM**

### **GENERAL DIAGNOSIS AND TREATMENT**

#### **Monday, November 7, 1938**

8:30 A. M.—9:00 A. M.	Registration	
9:00 A. M.	Welcome .....	GEORGE CRILE, M. D.
9:00 A. M.—9:30 A. M.	Diagnosis and Treatment of Cancer of the Uterus .....	T. E. JONES, M. D.
9:30 A. M.—10:15 A. M.	Symptoms and Treatment of Uri- nary Infection and Calculi .....	C. C. HIGGINS, M. D.
10:15 A. M.—11:00 A. M.	The Treatment of Colitis .....	E. N. COLLINS, M. D.
11:00 A. M.—11:45 A. M.	Importance of the Clinical His- tory in Genito-Urinary Diag- nosis .....	W. J. ENGEL, M. D.
11:45 A. M.—12:15 P. M.	Contact Dermatitis .....	GEO. H. CURTIS, M. D.
12:15 P. M.—1:30 P. M.	Luncheon	
1:30 P. M.—2:00 P. M.	Demonstration—"The Use of the Gastroscope" .....	R. J. RENSHAW, M. D.
2:00 P. M.—2:45 P. M.	Chronic Hoarseness .....	PAUL M. MOORE, M. D.
2:45 P. M.—4:00 P. M.	Low Back Pain—Differential Diagnosis and Treatment .....	JAMES A. DICKSON, M. D.
4:00 P. M.—5:00 P. M.	Management of Menopausal Symptoms .....	E. P. MCCULLAGH, M. D.
6:30 P. M.	Dinner	
8:00 P. M.	Frank E. Bunts Lecture	

#### **Tuesday, November 8, 1938**

9:00 A. M.—9:45 A. M.	Diagnosis and Treatment of De- ficiency Diseases .....	RUSSELL L. HADEN, M. D.
9:45 A. M.—10:45 A. M.	Physiotherapeutic Measures in the Treatment of Chronic Arthritis .....	WALTER J. ZEITER, M. D.
10:45 A. M.—11:30 A. M.	The Painful Shoulder .....	J. I. KENDRICK, M. D.

## Tuesday, November 8, 1938—Continued

- 11:30 A. M.—12:15 P. M. Some Problems in the Diagnosis  
and Treatment of Thyroid  
Diseases ..... R. S. DINSMORE, M. D.
- 12:30 P. M.— 1:30 P. M. Luncheon—Round Table
- 1:30 P. M.— 2:15 P. M. Treatment of Neurosyphilis with  
Special Reference to Its Pre-  
vention ..... E. W. NETHERTON, M. D.
- 2:15 P. M.— 3:00 P. M. The Drug Treatment of Heart  
Disease ..... A. C. ERNSTENE, M. D.
- 3:00 P. M.— 3:45 P. M. Differential Diagnosis and Treat-  
ment of Early Lesions of the  
Rectum ..... T. E. JONES, M. D.
- 3:45 P. M.— 4:15 P. M. Detection of Spinal Cord Lesions A. T. BUNTS, M. D.
- 4:15 P. M.— 5:00 P. M. Surgical Lesions of the Genito-  
Urinary Tract of General In-  
terest ..... W. E. LOWER, M. D.
- 6:30 P. M. Dinner  
Questions and Answers

## Wednesday, November 9, 1938

- 9:00 A. M.—10:00 A. M. Diagnosis and Treatment of  
Acute and Chronic Nephritis... R. H. McDONALD, M. D.
- 10:00 A. M.—10:30 A. M. Diagnostic Methods in Allergy... C. R. K. JOHNSTON, M. D.
- 10:30 A. M.—11:30 A. M. Problems Relating to Jaundice... RUSSELL L. HADEN, M. D.
- 11:30 A. M.—11:45 A. M. Surgical Aspects of Obstructive  
Jaundice ..... GEORGE CRILE, JR. M. D.
- 11:45 A. M.—12:30 P. M. Low-grade Fever — Causes and  
Treatment ..... JOHN TUCKER, M. D.
- 12:30 P. M.— 1:30 P. M. Luncheon
- 1:30 P. M.— 2:15 P. M. Lesions of the Chest Demon-  
strable by X-ray..... B. H. NICHOLS, M. D.
- 2:15 P. M.— 2:45 P. M. Tests and Treatment of Sterility.. GEORGE CRILE, JR., M. D.
- 2:45 P. M.— 3:15 P. M. Cerebral Pseudotumors—Condi-  
tions Simulating Brain Tu-  
mor and Brain Abscess..... W. JAMES GARDNER, M. D.
- 3:15 P. M.— 4:00 P. M. Differential Diagnosis and Treat-  
ment of Chronic Headache... CHARLES L. HARTSOCK, M. D.
- 4:00 P. M. The End Results of the Surgical  
Management of Essential Hy-  
pertension ..... GEORGE CRILE, M. D.
- Visit to Museum of Comparative  
Anatomy and Physiology.

# Exhibits

★ ★ ★

Transplantation of Endocrine Tissue .....	W. E. LOWER, M. D.
Urinary Calculi .....	C. C. HIGGINS, M. D.
The Hormones and Body Fluid .....	D. ROY McCULLAGH, PH.D.
Photographs of Dermatological Lesions .....	E. W. NETHERTON, M. D.
	AND GEO. H. CURTIS, M. D.
Roentgenograms of the Esophagus .....	PAUL M. MOORE, M. D.
Roentgenograms of Various Types of Chest Lesions .....	B. H. NICHOLS, M. D. AND
	J. C. ROOT, M. D.
Chronic Arthritis .....	RUSSELL L. HADEN, M. D. AND
	WALTER J. ZEITER, M. D.
Blood Dyscrasias .....	RUSSELL L. HADEN, M. D.
Roentgen Studies of Heart Lesions .....	A. C. ERNSTENE, M. D.
Fractures of the Hip .....	JAMES A. DICKSON, M. D.
Moulages of Lesions of the Hand .....	AND
Rupture of the Intervertebral Discs .....	J. I. KENDRICK, M. D.
Hyperthyroidism in the Extremes of Life .....	GEORGE CRILE, JR., M. D.
Endocrine Disturbances .....	E. P. McCULLAGH, M. D.
Carcinoma of the Colon and Rectum .....	T. E. JONES, M. D.
Lesions of the Gastro-Intestinal Tract .....	E. N. COLLINS, M. D.

## REGISTRATION BLANK

....., 1938

THE FRANK E. BUNTS INSTITUTE  
Cleveland Clinic  
Cleveland, Ohio

*Gentlemen:*

Please register me for the course in "Diagnosis and Treatment" which is to be given November 7, 8, and 9, 1938.

I am enclosing a check for \$5.00 and the remainder of the fee \$5.00, will be paid on registration, November 7.

Name .....

Address .....

Note: Checks should be made payable to The Frank E. Bunts Institute and sent to A. D. Ruedemann, M. D., Cleveland Clinic, Cleveland, Ohio.

.....  
Medical School from which Graduated

## THE FRANK E. BUNTS INSTITUTE

The Frank E. Bunts Institute, in conjunction with the Cleveland Ophthalmological Society, announces a course in Ophthalmology on December 5, 6, and 7, 1938.

On December 7, 8, and 9, a course in Diseases of the Ear, Nose, and Throat will be presented.

The program on Wednesday, December 7, is planned to be of interest to both the Ophthalmologist and the Otolaryngologist.

The fee for the two courses will be \$25.00. If only one course is taken, the fee will be \$15.00.

### PROGRAM

#### DISEASES OF THE EYE

##### Monday, December 5, 1938

8:30 A. M.— 9:00 A. M.	Registration
9:00 A. M.	Welcome
9:00 A. M.—10:00 A. M.	The Various New Cycloplegias
10:00 A. M.—11:00 A. M.	Results in the Treatment of Aniseikonia
11:00 A. M.—12:00 Noon	The Relation of the Eye Muscles to Ocular Discomfort— Methods of Treatment
12:00 Noon — 1:00 P. M.	Luncheon
1:00 P. M.— 1:30 P. M.	Exhibits Demonstrations
1:30 P. M.— 2:00 P. M.	Eye Glasses and Spectacles—the Value of Proper Fitting
2:00 P. M.— 3:00 P. M.	Refinements of Refraction
3:00 P. M.— 4:00 P. M.	Iritis—Differential Diagnosis and Treatment
4:00 P. M.— 5:00 P. M.	The Complications and Treatment of the Presbyopic Patient
6:00 P. M.	Dinner
8:00 P. M.	The Relation of Arthritis to Eye Conditions

#### DISEASES OF THE EYE

##### Tuesday, December 6, 1938

9:00 A. M.—10:00 A. M.	Perimetric Studies and Encephalograms; Diagnostic Value of Perimetric Studies
10:00 A. M.—11:00 A. M.	The Selection of Surgery in Glaucoma
11:00 A. M.—12:00 Noon	Relation between Clinical Findings
12:00 Noon— 1:00 P. M.	Luncheon
1:00 P. M.— 1:30 P. M.	Exhibits Demonstrations
1:30 P. M.— 2:00 P. M.	Further Studies with Ocular Illusions
2:00 P. M.— 3:00 P. M.	Vascular Disease of the Retinae—Clinical and Experimental
3:00 P. M.— 4:00 P. M.	The Preparation of the Patient for Cataract Surgery
4:00 P. M.— 5:00 P. M.	The Etiology and Treatment of the Protruding Inflammatory Eye
6:00 P. M.	Dinner
8:00 P. M.	REGULAR MEETING CLEVELAND OPHTHALMOLOGICAL CLUB

## DISEASES OF THE EYE, EAR, NOSE, AND THROAT

### Wednesday, December 7, 1938

- 8:30 A. M.— 9:00 A. M. Registration for Course in Diseases of the Ear, Nose, and Throat
- 9:00 A. M. Welcome ..... GEORGE CRILE, M. D.,  
Cleveland Clinic.
- 9:00 A. M.—10:00 A. M. The Use of Short-Wave Diathermy in Eye, Ear, Nose, and Throat—deep and superficial ..... WALTER J. ZEITER, M. D.,  
Cleveland Clinic.
- 10:00 A. M.—11:00 A. M. The Use of X-ray Therapy in Eye, Ear, Nose, and Throat ..... U. V. PORTMANN, M. D.,  
Cleveland Clinic.
- 11:00 A. M.—12:00 Noon Medical Aspects of Dental Infection ..... RUSSELL L. HADEN, M. D.,  
Cleveland Clinic.
- 12:00 Noon— 1:00 P. M. Luncheon
- 1:00 P. M.— 2:00 P. M. Diagnostic Methods in Allergy ..... C. R. K. JOHNSTON, M. D.,  
Cleveland Clinic.
- 2:00 P. M.— 3:00 P. M. Chronic Headaches ..... CHARLES L. HARTSOCK,  
M. D., Cleveland Clinic.
- 3:00 P. M.— 4:00 P. M. Chronic Fever—Use of Typhoid Therapy ..... JOHN TUCKER, M. D.,  
Cleveland Clinic.
- 4:00 P. M.— 5:00 P. M. Chronic Bronchitis ..... A. CARLTON ERNSTENE,  
M. D., Cleveland Clinic.
- 6:00 P. M. Dinner
- 8:00 P. M. Mullin Lecture:  
"My Son Studies Medicine" ..... W. P. WHERRY, M. D.,  
Professor of Otorhino-  
laryngology, University  
of Nebraska, College of  
Medicine, Omaha, Ne-  
braska.

## DISEASES OF THE EAR, NOSE, AND THROAT

### Thursday, December 8, 1938

- 9:00 A. M.—10:00 A. M. Sulfanilamide Therapy ..... PAUL M. MOORE, M. D.,  
Cleveland Clinic.
- 10:00 A. M.—11:00 A. M. The Differential Diagnosis of Cough ..... GEORGE L. KING, M. D.,  
Alliance, Ohio.
- 11:00 A. M.—12:00 Noon Points of Practical Interest in the Diagnosis, Time of Operations, and Treatment in Ear Conditions, Including Mastoid, Lateral Sinus, Labyrinth, Meningeal and Petrous Infections (Part 1) ..... HENRY GOODYEAR, M. D.,  
Cincinnati, Ohio.
- 12:00 Noon— 1:00 P. M. Luncheon
- 1:00 P. M.— 2:00 P. M. Exhibits
- 2:00 P. M.— 3:00 P. M. Points of Practical Interest in the Diagnosis, Time of Operations, and Treatment in Ear Conditions, Including Mastoid, Lateral Sinus, Labyrinth, Meningeal and Petrous Infections (Part 2) ..... HENRY GOODYEAR, M. D.,  
Cincinnati, Ohio.
- 3:00 P. M.— 4:00 P. M. The Comparative Anatomy of the Larynx ..... W. LORNE DEETON, M. D.,  
Cleveland Clinic.
- 4:00 P. M.— 5:00 P. M. Laryngeal Neuroses ..... JUSTIN M. WAUGH, M. D.,  
Cleveland Clinic.
- 6:00 P. M. Dinner  
"Questions and Answers."



## DISEASES OF THE EAR, NOSE, AND THROAT—Continued

Friday, December 9, 1938

9:00 A. M.—10:00 A. M. Vertigo .....	W. LORNE DEETON, M. D., Cleveland Clinic.
10:00 A. M.—11:00 A. M. Esophageal Lesions .....	J. H. MAXWELL, M. D., Ann Arbor, Michigan.
11:00 A. M.—12:00 Noon Sore Throat .....	I. F. WEIDLEIN, M. D., Cleveland, Ohio.
12:00 Noon— 1:00 P. M. Luncheon	
1:00 P. M.— 2:00 P. M. Exhibits	
2:00 P. M.— 3:00 P. M. The Complications of Acute Sup- purative Otitis Media .....	J. H. MAXWELL, M. D., Ann Arbor, Michigan.
3:00 P. M.— 4:00 P. M. The Infant Mastoid—Development, Infections, Treatment .....	PAUL M. MOORE, M. D., Cleveland Clinic.
4:00 P. M.— 5:00 P. M. Interesting Case Reports .....	HAROLD E. HARRIS, M. D., and LLOYD P. WARREN, M. D., Cleveland Clinic.

### REGISTRATION BLANK

THE FRANK E. BUNTS INSTITUTE  
Cleveland Clinic  
Cleveland, Ohio

....., 1938

Gentlemen:

☐ Please register me for the courses in Ophthalmology and Otolaryngology which are to be given December 5, 6, 7, 8, 9, 1938. I am enclosing a check for \$5.00 and the remainder of the fee, \$20.00, will be paid on registration, December 5.

☐ Please register me for the course in Ophthalmology which is to be given on December 5, 6, 7, 1938. I am enclosing a check for \$5.00, and the remainder of the fee, \$10.00, will be paid on registration, December 5.

☐ Please register me for the course in Otolaryngology which is to be given December 7, 8, 9, 1938. I am enclosing a check for \$5.00 and the remainder of the fee, \$10.00, will be paid on registration, December 7.

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Name .....

Address .....

.....  
Medical School from which Graduated.

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